









# CHEMICAL REVIEWS

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# RECENT PROGRESS IN DETERMINING THE CHEMICAL STRUCTURE OF CHLOROPHYLL

CATHERINE C. STEELE<sup>1</sup>

*Received November 30, 1936*

## I. INTRODUCTION

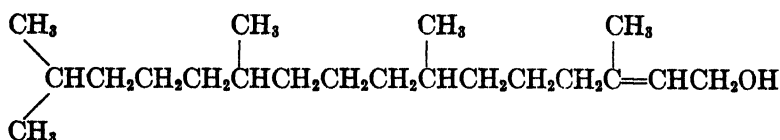
The name "chlorophyll" was first given by Pelletier and Caventou (1817) to the green coloring material in the chloroplasts of plant leaves; it was not, however, until much later that extensive chemical investigations were made on the pigment. In 1864 the English physicist Stokes (81) showed spectroscopically that the chloroplast pigment was a mixture, and Sorby (76) separated it into four pigments, two yellow and two green, by partition between immiscible solvents. This work was ignored until Willstätter (1906) repeated and extended the investigation. In the intervening years many attempts were made to isolate the chloroplast pigments; the isolation of two yellow pigments was repeated by several investigators, but the use of too drastic methods gave very impure chlorophyll extracts, so that, for instance, one worker reported that from a single plant species alone he had obtained some twenty different chlorophylls.

From 1906 to 1914 Willstätter (98) and his collaborators not only succeeded in preparing pure chlorophyll for the first time, but their chemical investigations laid the foundation of our present knowledge of the structures of the green pigments. Willstätter showed that there were two green pigments, chlorophylls *a* and *b*, present in all plant leaves, and that they could be separated by the preferential solubility of chlorophyll *a* in petroleum ether and of chlorophyll *b* in 90 per cent methyl alcohol. The later method devised by Winterstein and Stein (100) of chromatographic adsorption of the pigments on powdered sugar affords an even simpler means of separation. Willstätter found that the ratio of chlorophyll *a* to chlorophyll *b* was remarkably constant in the higher plants, being about three to one. The function of the chlorophylls in the photosynthetic process will not be considered in this paper; reviews, e.g. those of Spoehr (77) and of Stoll (83), and physiological textbooks may be consulted.

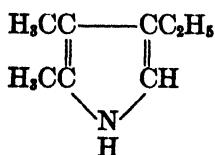
<sup>1</sup> Ph.D. (St Andrews); former Commonwealth Fund Fellow at the University of Illinois and at Harvard University. Present address: 301 Hartel Street, Philadelphia.

Chlorophyll and its derivatives are very sparingly soluble in organic solvents and are difficult to purify. The chief means of identifying individual compounds is by their unique absorption spectra. Willstätter introduced a general method for the separation and purification of chlorophyll derivatives; they were extracted from ether with hydrochloric acid of different concentrations. This method of acid fractionation depends on the large differences in the distribution ratios of these substances between ether and dilute acid, brought about by small differences in basicity and in solubility. Chlorophyll derivatives are therefore all characterized by an *acid number*, defined as that percentage concentration of hydrochloric acid which extracts two-thirds of the substance from an equal volume of an ether solution.

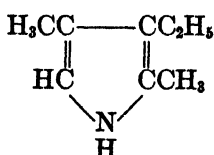
Willstätter determined the correct empirical formula for chlorophyll *a* as  $C_{55}H_{72}N_4O_6Mg$  (later substantiated by Fischer (15) and by Stoll (82)), and found that chlorophyll *b* contained an additional oxygen atom, and two hydrogens less than *a*. He proved for the first time the presence of magnesium in the chlorophyll molecule, and showed that in physical properties and indeed to some extent in chemical nature chlorophyll was a wax. On hydrolysis it yields two alcohols, methyl alcohol and phytol,  $C_{20}H_{39}OH$ . The latter, by the brilliant synthesis of Gottwalt Fischer (14), was shown to have the following structural formula:



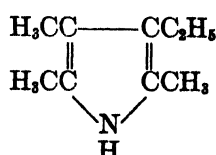
The earliest obtained derivatives of chlorophyll were the pyrroles and the porphyrins. Nencki (72) and later Willstätter (95) reduced chlorophyll to substituted pyrroles, identified by the latter investigator as hemopyrrole, kryptopyrrole, and phyllopyrrole:



I a  
Hemopyrrole

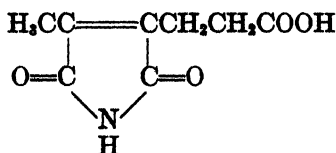


I b  
Kryptopyrrole

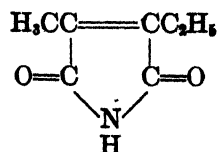


I c  
Phyllopyrrole

Kuster (68) obtained pyrroles by the oxidative degradation of chlorophyll, and isolated hematinic acid and methylethylmaleic imide:



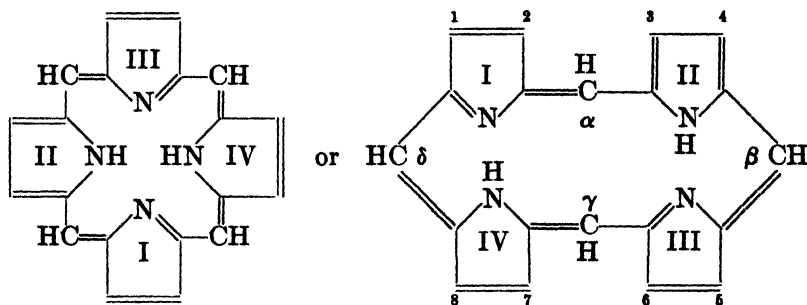
II a  
Hematinic acid



II b  
Methylethylmaleic imide

Hemoglobin, on reduction and oxidation respectively, gives the same series of pyrroles.

Again, both pigments on drastic alkaline degradation give porphyrins, red, crystalline compounds with characteristic absorption spectra. These porphyrins were originally obtained by Hoppe-Seyler (67) and also by Schunck (75). Indeed, this formation of porphyrins was the first indication of a similarity in chemical structure between the blood pigment and chlorophyll. In the chlorophyll series of porphyrins, Willstätter characterized the dicarboxylic acid rhodoporphyrin, the monocarboxylic acids phylloporphyrin and pyrroporphyrin, and the oxygen-free compound pyrroetioporphyrin. Porphyrins all contain four pyrrole nuclei, and Kuster (69) suggested that these were arranged in a symmetrical fashion according to the following skeletal structure.



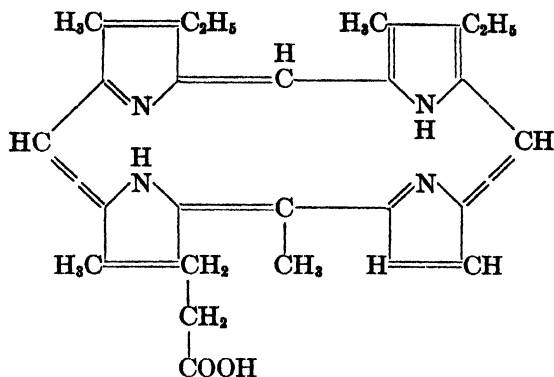
III  
The porphin nucleus

This unsubstituted nucleus, termed the *porphin* nucleus, possesses a conjugated system similar to that of benzene, and hence the distribution of the double bonds is admittedly arbitrary. Since the second alternative method of writing the nucleus is that at present in use by Hans Fischer, it will be adopted in this review for the sake of uniformity.

In a series of publications extending over some twenty years, Hans Fischer has proved by synthesis that Kuster's formulation for the porphyrin nucleus was correct.







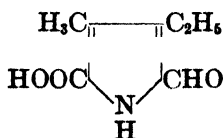
Vc

Phylloporphyrin

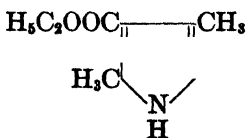
Phylloporphyrin, which contains a methyl group on the  $\gamma$ -bridge carbon atom (see formula III for the system of numbering), can be converted into pyrrorporphyrin by the action of sodium ethoxide.

Rhodoporphyrin, as shown above, possesses besides a propionic acid group in position 7 a carboxyl group in the 6-position, which is occupied by the unsubstituted hydrogen atom in pyrro- and phyllo-porphyrins. In systematic nomenclature, rhodoporphyrin is 1,3,5,8-tetramethyl-2,4-diethyl-6-carboxyporphin-7-propionic acid. The length of these systematic names has precluded their use for the various degradation products of chlorophyll in favor of the unsystematic names given by Willstätter, but they are retained by Fischer for the purely synthetic methenes and porphins.

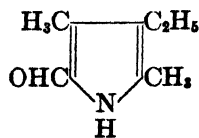
The synthesis of rhodoporphyrin is outlined below to show the general method for porphyrin synthesis. The ethyl ester of the 5-carboxy derivative of kryptopyrrole (I b), treated with three molecules of sulfuryl chloride, gives as one of the products 2-formyl-3-ethyl-4-methylpyrrole-5-carboxylic acid (VI a). This is condensed with the ethyl ester of 3,5-dimethylpyrrole-4-carboxylic acid (VI b) by trituration in the presence of hydrogen bromide and glacial acetic acid. The dipyrromethene so obtained is the 4-ethyl ester of 3,5,4'-trimethyl-3'-ethylpyrromethene-4,5'-dicarboxylic acid (VII A). In numbering the positions in the dipyrromethenes, the 2 and 2' positions are always those occupied by the methene bridge.



VI a



VI b



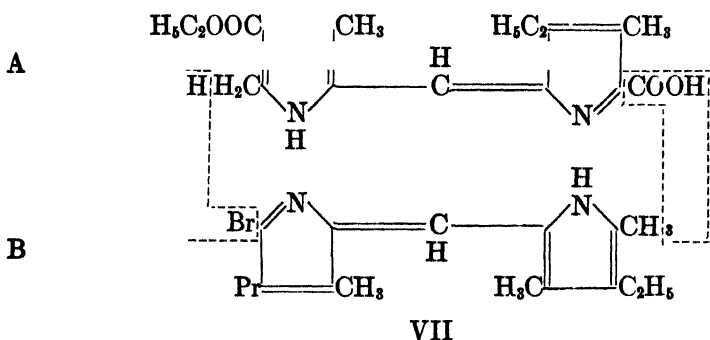
VI c



VI d

(Pr = propionic acid)

Similarly from 5-formylkryptopyrrole (VI c) and the ethyl ester of 4-methylpyrrole-3-propionic acid (VI d) is obtained the dipyrromethene, 3,5,3'-trimethyl-4-ethylpyrromethene-4'-propionic acid (VII B; H in place of Br). Compound B is obtained by bromination of the hydrobromide of this dipyrromethene with free bromine at 50° to 60°C. It is then condensed with the hydrobromide of A by melting the mixture over a free flame in the presence of succinic acid. Condensation occurs as indicated by the dotted lines in the following formulas, and fractionation of the product leads to the isolation of rhodoporphyrin (Va).



In all such syntheses, each of the methenes can react with itself, and therefore other porphyrins are always present. Further, decarboxylation frequently occurs, resulting in more porphyrins, and the isolation of the required porphyrin is often difficult. Therefore the proof of the structure of a given porphyrin rests not alone on the synthesis, but on that coupled with the knowledge of its structure derived from degradation reactions.

Unsubstituted porphyrin (III) itself has also been synthesized. Fischer (29) condensed in one step four molecules of 2-pyrrolealdehyde by means of boiling formic acid in the presence of alcohol to give porphyrin. Rothmund (73) prepared porphyrin by condensing pyrrole with an equimolecular proportion of formaldehyde. When other aldehydes were used, then porphyrins substituted in the  $\alpha$ -,  $\beta$ -,  $\gamma$ -, and  $\delta$ -positions were obtained.

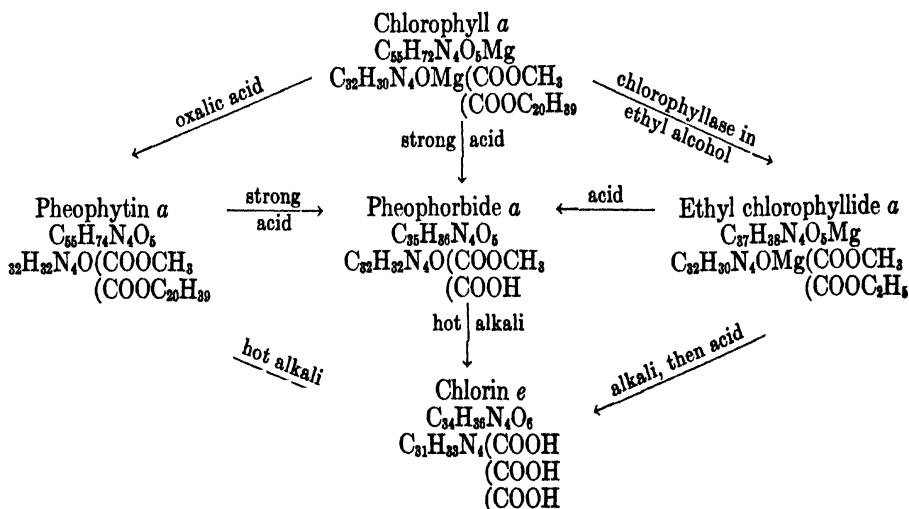
III. CHLOROPHYLL *a*

## INVESTIGATIONS OF WILLSTÄTTER

Willstätter prepared a number of derivatives by the action of acid and of alkali on chlorophyll *a*. Chlorophyll, on careful treatment with oxalic acid, loses magnesium, and yields a waxy substance called pheophytin. This has no acid properties, and therefore the magnesium cannot be present as a salt, but must be attached to nitrogen. Hydrolysis of pheophytin with strong acid removes phytol, yielding pheophorbide *a*, a mono-methyl ester of a dicarboxylic acid. Esterification with diazomethane gives the dimethyl ester, methyl pheophorbide *a*.

If sections of the green leaves of certain plants (e.g., *Heracleum sphondylium*) are soaked in alcohol, large crystals are developed in the chloroplasts; the substance concerned was called "crystalline chlorophyll." Willstätter showed that these plants contain an enzyme, chlorophyllase, which hydrolyzes the phytol group and replaces it by the alcohol present. The products are therefore now called ethyl chlorophyllide, if ethyl alcohol is used, methyl chlorophyllide from methyl alcohol, and so forth.

Saponification of pheophorbide *a* or of its ester with hot alkali yields phytychlorin *e* (usually abbreviated to chlorin *e*), which gives with diazomethane a trimethyl ester, according to Treibs and Wiedemann (91). These reactions of chlorophyll are summarized as follows:



## VIII

After the brilliant syntheses of the chlorophyll porphyrins by Hans Fischer, the relationship of the structure of chlorophyll to the porphyrin

nucleus and the nature of the labile groups in chlorophyll required elucidation. The problem was taken up almost simultaneously by Fischer and by J. B. Conant. It seems advisable to separate to some extent the account of the work of these investigators, but in each case historical sequence will not necessarily be observed, for reasons of brevity.

#### INVESTIGATIONS OF CONANT

##### *The phytol group*

Conant (7, 5) first correctly placed the phytol group in chlorophyll on the propionic acid side chain. Pheophorbide *a* contains a methoxyl group derived unchanged from chlorophyll *a* (VIII), and a free acid residue resulting from the loss of phytol through hydrolysis. On pyrolysis, pheophorbide *a* is converted into pyropheophorbide *a*, which has lost a methoxyl group, but still retains a carboxylic acid group; the latter acid group must be the propionic acid residue, otherwise it would be eliminated in the pyrolysis. Hence the propionic acid group which survives pyrolysis must be esterified with phytol in the chlorophyll molecule. Fischer later provided an independent proof of this in the hydrogen iodide reactions (*vide infra*).

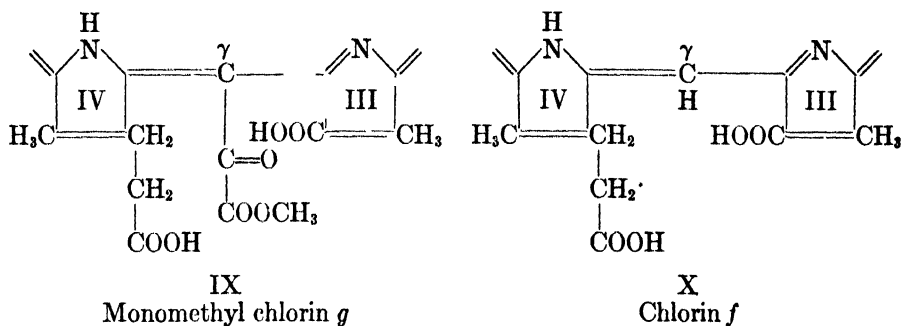
##### *The phase test*

Willstätter found that a characteristic reaction of chlorophyll, pheophytin, and pheophorbide in ether solution is the sequence of color changes (green, then yellow, reverting to green, in the *a* series) obtained by the action of cold alcoholic alkali. Conant (11) found that the first product of the "phase test" reaction is an unstable chlorin (apparently identical with Willstätter's (99) phytochlorin *g*), which on being allowed to stand is converted into pheopurpurin 18, a substance with a vivid purple color in ether solution and of "acid number" 18. Immediate esterification of the reaction mixture converts the unstable chlorin into dimethyl pheopurpurin 7. Dimethyl pheopurpurin 7 (a trimethyl ester) on careful hydrolysis loses two methyl groups, forming pheopurpurin 7, a monomethyl ester.

This phase test reaction was shown by Conant (10, 78) to be an oxidative hydrolysis, with atmospheric oxygen acting as hydrogen acceptor. Still milder conditions of oxidative hydrolysis (4) result in a stable chlorin, which is a monomethyl ester. Hydrolysis of this ester yields the unstable chlorin, hence the former is monomethyl chlorin *g* (IX), while diazomethane further esterifies it directly to dimethyl pheopurpurin 7.

Hot saponification of either pheopurpurin 7 or its ester (8, 5) gives rise to a new chlorin (X), chlorin *f* (which Fischer later prepared and called rhodochlorin). Reduction of this dibasic acid with hydrogen iodide in

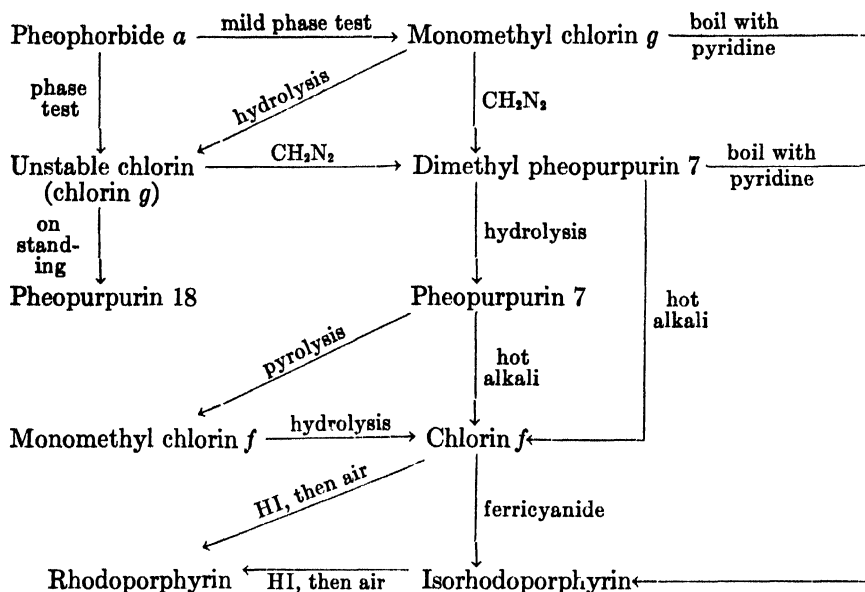
acetic acid, and subsequent re-oxidation in air, results in the formation of the dibasic acid, rhodoporphyrin (Va). Since the latter contains no side chain on the  $\gamma$ -bridge carbon atom, neither does chlorin *f*. Chlorin *f* therefore contains a carboxyl group in the 6-position, and a propionic acid residue in the 7-position, according to the partial formula (X; see also XXVIII a, and XXIX a and b).



Direct dehydrogenation of chlorin *f*, using ferricyanide in an alkaline solution at room temperature (8), gives not rhodoporphyrin but isorhodoporphyrin, which differs from chlorin *f* by containing two hydrogen atoms less. This same porphyrin can also be obtained more directly from pheopurpurin 7; Conant (2) found that pyrolysis of the latter yields small amounts of the porphyrin, while Fischer (66) prepared it by heating dimethyl pheopurpurin 7 in pyridine. He called it pseudoverdoporphyrin, since it also appeared to be isomeric with a verdoporphyrin obtained from the decomposition of chlorophyll by Treibs and Wiedemann (91). This "verdoporphyrin" has now been shown by Fischer (40) to be a mixture of porphyrins. Isorhodoporphyrin can be readily converted into rhodoporphyrin by reduction with hydrogen iodide, followed by atmospheric oxidation. Their relationship is discussed more fully later.

The schematic representation of the phase test products is shown on page 10.

If the isorhodoporphyrin molecule is represented by P, then chlorin *f* is PH<sub>2</sub>. Hence according to Conant (2), the fundamental nuclear structure of the pheophorbides and of chlorophyll *a*, which is that of chlorin *f*, is also a dihydroisorhodoporphyrin ring. This result had been foreshadowed by Conant and Kamerling (9), who studied the visible absorption spectra of these compounds at liquid air temperatures. Porphyrins under such conditions show a unique pattern of groups of narrow bands, comparable to the ultra-violet absorption spectrum of benzene, for instance. On the other hand, chlorophyll derivatives such as the pheo-

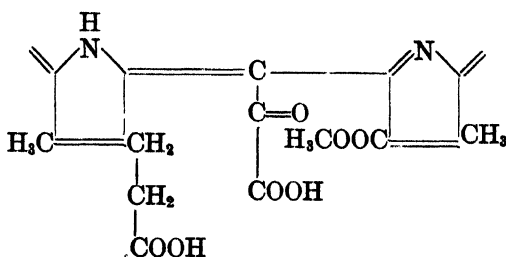


## XI

## The phase test products

phorbides and the chlorins have spectra with wider bands similar to the spectrum of cyclohexadiene (dihydrobenzene).

In the saponification of pheopurpurin 7 to chlorin *f* ( $\text{PH}_2$ ), oxalic acid is also obtained, hence pheopurpurin 7 (and the isomeric unstable chlorin) is represented by  $\text{PH}_2\text{C}_2\text{O}_3$ . Again, pyrolysis of pheopurpurin 7 (a monomethyl ester) produces the monomethyl ester of chlorin *f*, accompanied by the evolution of carbon dioxide and carbon monoxide. Hence pheopurpurin 7 contains an  $\alpha$ -keto acid (or glyoxalic acid) residue on the  $\gamma$ -bridge carbon atom, and may be represented by the following partial formula (8, 12):



## XII

## Pheopurpurin 7

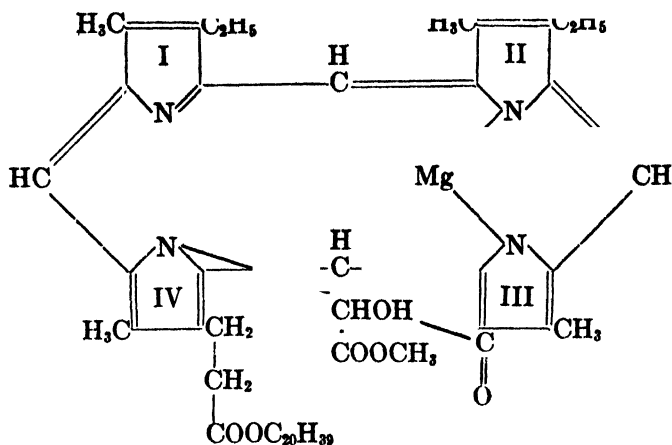
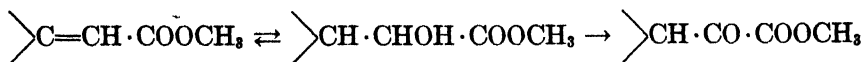
Fischer placed the methyl group in chlorophyll *a* and pheophorbide *a* on the side chain of the  $\gamma$ -bridge carbon atom as a carbomethoxyl residue (*vide infra*). Conant originally placed it on the 6-carboxyl, but later corroborated Fischer's result by independent evidence (4). Monomethyl chlorin *g* (IX) can be esterified with diazoethane to give diethyl pheopurpurin 7 (a diethyl monomethyl ester). If the latter is heated with pyridine the methoxyl is lost, and there results a diethyl ester of isorhodoporphyrin, which has no substituent on the  $\gamma$ -bridge. Hence the methoxyl must be part of the  $\gamma$ -bridge grouping in monomethyl chlorin *g*. If the latter is subjected to pyrolysis, methoxyl-free isorhodoporphyrin is formed, hence again in monomethyl chlorin *g*, and therefore also in chlorophyll and pheophorbide, the methoxyl is in the  $\gamma$ -bridge grouping.

### *Allomerization*

Willstätter described a reaction of chlorophyll which he termed allomerization. When an alcoholic solution of chlorophyll is allowed to stand for some time, the resulting material, "allomerized chlorophyll," is no longer capable of giving the phase test. From the alcoholic solution he prepared phytychlorin *g* (99). Conant (8) showed that "allomerized chlorophyll" on hydrolysis, removal of magnesium by acid, and esterification with diazomethane, gives the same product—dimethyl pheopurpurin 7—as does the phase test. This is in contrast with unallomerized chlorophyll, which under identical treatment yields the trimethyl ester of chlorin *e* (VIII). That allomerization is an oxidative reaction was shown by Conant (10) using a modified Warburg apparatus; two equivalents of oxygen are absorbed per mole of chlorophyll. He further found that chlorophyll and the pheophorbides can be dehydrogenated (5), using two equivalents of potassium molybdicyanide, and again dimethyl pheopurpurin 7 is obtained. Hence the phase test, allomerization, and direct dehydrogenation all lead through dimethyl pheopurpurin 7 and chlorin *f* to isorhodoporphyrin, or to rhodoporphyrin, while rapid saponification, which excludes oxidation, results in chlorin *e* (VIII), from which phylloporphyrin is derived. To explain these results, Conant (4) suggested a structure for chlorophyll (XIII) which has a dihydroporphyrin nucleus, and an esterified lactic acid side chain on the  $\gamma$ -bridge carbon atom. To account for the fact that although crystallized chlorophyll *a* has only five oxygen atoms, it has two ester groups and a potential carboxyl group in the 6-position (which appears in chlorin *e*), two further postulates were made:—*viz.*, that a lactam bridge is present between the potential carboxyl group and the nitrogen atom in pyrrole ring IV, and that the secondary alcoholic grouping in the lactic acid side chain was dehydrated, at least in crystallized chlorophyll. The dehydrogenation results are ex-



plained by the hydration of this unsaturated linkage, followed by oxidation to the  $\alpha$ -keto grouping (1):



XIII  
Chlorophyll *a* (Conant, 1933)

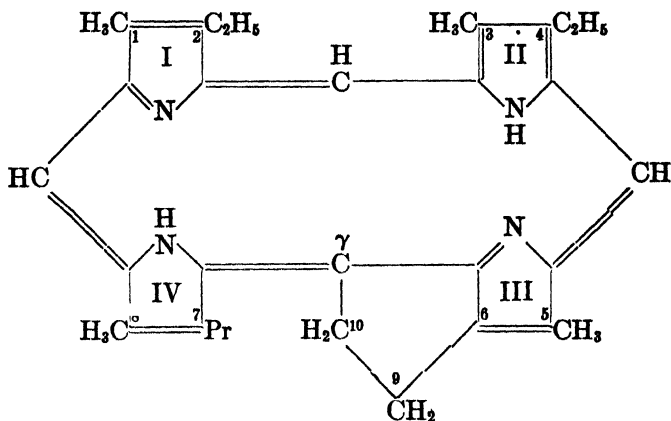
#### INVESTIGATIONS OF FISCHER

##### *The carbocyclic (or isocyclic) ring*

Fischer found a mild reagent for the degradation of chlorophyll in glacial acetic acid solutions of hydrogen iodide at 50°C. By such treatment, many chlorophyll derivatives are reduced to colourless leuco compounds, which re-oxidize in air to porphyrins (47, 18, 65, 48); these, however, unlike the chlorophyll porphyrins previously described, retain the full carbon skeleton of the original compound. In this manner the pheophorbides give rise to pheoporphyrins, while chlorin *e* gives rise to a different series, the chloroporphyrins. Thus pheophorbide *a* with hydrogen iodide yields pheoporphyrin *a*<sub>6</sub> (65); this contains, like the parent compound, a carbomethoxyl group and a carboxyl group. Further treatment with hydrogen iodide, or the action of hydrogen bromide in acetic acid, eliminates the carbomethoxyl group, giving phylloerythrin, which is spectroscopically a porphyrin. Phylloerythrin may also be obtained directly from pheophorbide *a*, and from pheophytin and the chlorophyllides, by refluxing with 20 per cent hydrochloric acid.

Now phylloerythrin,  $\text{C}_{33}\text{H}_{34}\text{O}_2\text{N}_4$ , was already known as a biological decomposition product of chlorophyll; Löbisch and Fischler (70), finding it in ox bile, called it bilipurpurin, while Marchlewski (71) isolated it from

the feces of herbivora. These biological sources of phylloerythrin convinced Fischer that the hydrogen iodide treatment was mild, and that chlorophyll, the phorbides, and phylloerythrin were closely related in chemical structure. Phylloerythrin contains a reactive carbonyl group which forms an oxime, and which can be reduced by the Wolff-Kishner method (the action of hydrazine and sodium ethoxide in a sealed tube) to form desoxophylloerythrin (48). This compound, a porphyrin with one carboxylic acid group, may also be prepared directly from pheophytin *a* or from pheophorbide *a*, by the action of hydrogen bromide in acetic acid at 180°C. (49). Fischer determined the structure of desoxophylloerythrin by synthesis (51). It is represented by the following formula:



XIV

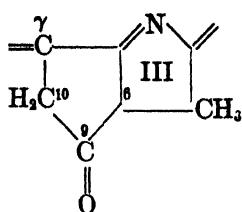
Desoxophylloerythrin



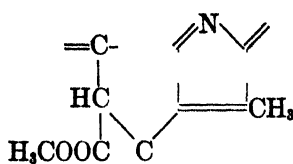
Desoxophylloerythrin can be oxidized with oleum and sulfur to regenerate phylloerythrin. That the carbonyl group in phylloerythrin (XV) is in position 9 and not 10 follows from its alkaline decomposition to rhodoporphyrin, containing a carboxyl group in position 6 (Va).

The structure of pheoporphyrin *a*<sub>6</sub> (49) is established by its relationship to phylloerythrin and to the chloroporphyrins. Pheoporphyrin *a*<sub>6</sub> contains a carbomethoxyl group, that is, it always occurs as the monomethyl ester. It contains in addition a carbonyl group, and on hydrolysis yields chloroporphyrin *e*<sub>6</sub> (XVII), so-called because it is obtainable by the action of hydrogen iodide on chlorin *e* trimethyl ester. Chloroporphyrin *e*<sub>6</sub> is the monomethyl ester of rhodoporphyrin- $\gamma$ -acetic acid. Formic acid converts it to  $\gamma$ -methylrhodoporphyrin (chloroporphyrin *e*<sub>4</sub>), and this in turn can be converted to phylloporphyrin (Vc). Pheoporphyrin *a*<sub>6</sub> (XVI)

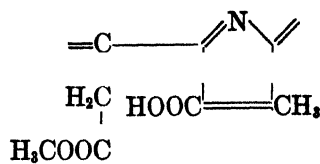
therefore contains the carbocyclic ring of phyloerythrin with a carbo-methoxyl group in position 10.



XV  
Phylloerythrin

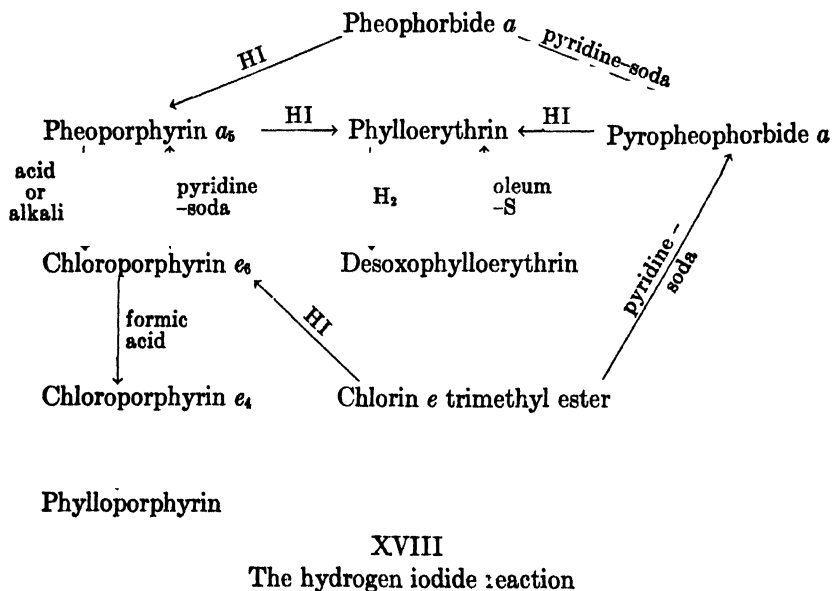


XVI  
Pheoporphyrin  $a_6$



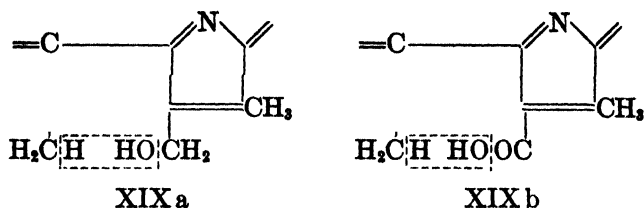
XVII  
Chloroporphyrin  $e_6$

The following table summarizes some of these relationships. For a more complete discussion of the pheo- and chloro-porphyrins, two summaries by Fischer may be consulted (16).



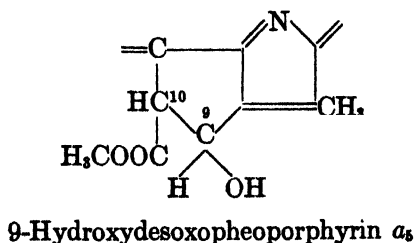
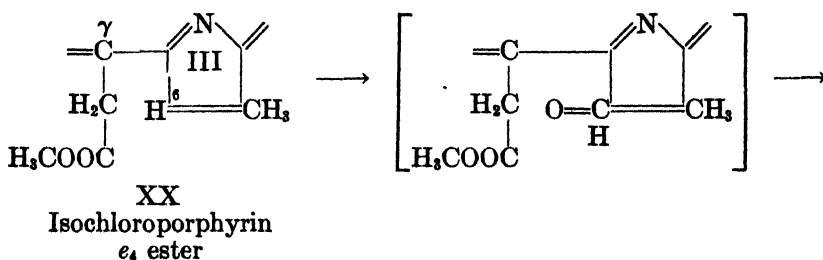
Other proofs of the position of the carbonyl group in position 9 in pheoporphyrin  $a_6$  and in phylloerythrin have been found through partial synthesis of these substances. Desoxophylloerythrin has been obtained by ring closure (59) between positions 6 and  $\gamma$  in 6-hydroxymethylphylloporphyrin (XIX a). The latter is obtained from phylloporphyrin by the action of bromine, to yield 6-bromophylloporphyrin, followed by

treatment with methyl alcoholic alkali, which converts the bromine to the primary alcoholic group ( $-\text{CH}_2\text{OH}$ ). Similarly phyloerythrin was obtained by a condensation between positions 6 and  $\gamma$  in chloroporphyrin  $e_4$  ( $\gamma$ -methylrhodoporphyrin) under the influence of sodium ethylate (XIX b) (50).



This extreme ease of formation of the carbocyclic ring is actually comparable with the methods employed by Fischer in converting the pheophorbides to substances such as phyloerythrin and desoxyphyloerythrin, where the existence of the carbocyclic ring has been definitely established by synthesis. Even in view of the biological data cited above, it would appear that the presence of the carbocyclic ring in pheophorbide and in chlorophyll has not yet been unequivocally proved.

Again, esterification of chlorin  $e$  by means of methyl alcohol and hydrochloric acid gives a diester in which the carboxyl group in the 6-position is free. This diester on pyrolysis loses the carboxyl group, and subsequent catalytic reduction to the leuco compound, followed by re-oxidation in air, gives rise to isochloroporphyrin  $e_4$  diester (XX) (41). Here position



6 is unsubstituted, and the  $\gamma$ -carbon atom possesses an acetic ester residue. Fischer found means of introducing the formyl group into porphyrins by treating the hemin (complex iron salt) of the porphyrin with dichloromethyl ether in the presence of stannic chloride or bromide (57). In this instance the formyl group enters at position 6, and ring closure (a Claisen condensation) takes place spontaneously, so that the product isolated is 9-hydroxydesoxopheoporphyrin  $a_5$  (42). The latter compound was already known; it is obtainable by catalytic hydrogenation of pheoporphyrin  $a_5$  (34).

If isochloroporphyrin  $e_4$  ester is brominated, one atom of bromine enters the molecule apparently in position 6, for on heating the brominated compound above its melting point, ring closure is effected with the formation of phylloerythrin.

If the formyl group is introduced into phylloporphyrin (Vc) by the method outlined above, the ester of the resulting 6-formylphylloporphyrin gives rise to an interesting series of 9-substituted derivatives of desoxyphylloerythrin methyl ester (50), by the same type of ring closure. For instance, 6-formylphylloporphyrin ester condensed with malonic acid gives the 9-acetic acid derivative of desoxyphylloerythrin ester, while with methyl alcohol and concentrated hydrochloric acid, the 9-methoxy derivative is obtained.

Conant (7) attempted the pyrolysis of several chlorophyll derivatives in diphenyl, and from the results obtained from methyl pheophorbide  $a$  established the position of the phytol group. Fischer (27) found better conditions for pyrolysis in the use of pyridine and sodium carbonate. If pheophorbide is so treated, the carbomethoxyl group is eliminated. The product is pyropheophorbide  $a$ , containing a carbonyl group in a carbocyclic ring, and spectroscopically a phorbide, but isomeric with phylloerythrin, into which it is convertible by treatment with hydrogen iodide. Fischer isolated from sheep feces (37) a mixture of degradation products of chlorophyll. The name probophorbide was used for some of these, but later (62) phylloerythrin, pyropheophorbide  $a$ , and its dihydro derivative were isolated from the mixture. It should be noted (XVIII) that pyrolysis of chlorin  $e$  trimethyl ester also results in pyropheophorbide (58). In this case, synthesis of a carbocyclic ring has taken place, and a similar synthesis occurs in the pyrolysis of chloroporphyrin  $e_4$  to pheoporphyrin  $a_5$ .

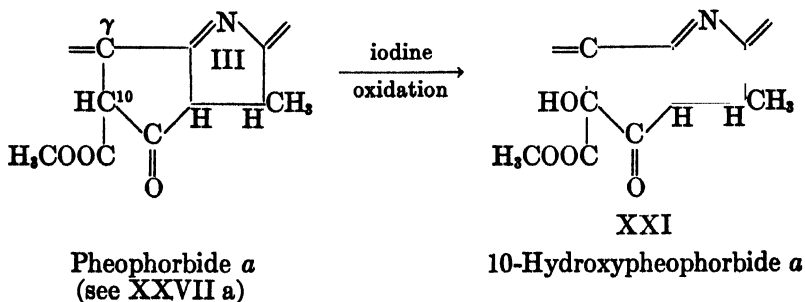
The carbocyclic rings of pyropheophorbide  $a$  and of phylloerythrin are the same, and according to Fischer pheophorbide  $a$  and pheoporphyrin  $a_5$  form a similar pair. This latter identity Fischer deduced from the relationships outlined in the preceding paragraphs, and from the following additional facts. The chlorophyllides, methyl pheophorbide, and pheo-

phorbide at ordinary temperatures in an atmosphere of nitrogen form oximes (53), which analyze as substitution, not addition, products and hence show the presence of a carbonyl group. The original compounds can be regenerated from the oximes, and the latter are converted by hydrogen iodide into the oxime of pheoporphyrin  $a_5$ . The enolic modification must also be possible, since methyl pheophorbide and pheophorbide form benzoyl substitution products, as was shown by Stoll (87). The  $\beta$ -ketonic acid grouping ( $R \cdot CO \cdot CHR' \cdot COOCH_3$ ) of the carbocyclic ring admits of these modifications, and also explains the reaction of chlorophyll and the pheophorbides to acid and to hot alkali. The latter hydrolyzes the ester groups and opens the carbocyclic ring with the formation of chlorin  $e$  (XXIII); acid, on the other hand, in addition to hydrolysis of the ester groups, removes carbon dioxide from the carbomethoxyl group, leading to phylloerythrin. Again, Stern and Klebs (79) conducted calorimetric investigations on chlorophyll derivatives, and concluded that the energy values of pheophorbide  $a$  and of pheoporphyrin  $a_5$  were the same, indicating that they were isomeric. But it is doubtful if a small difference, e.g., of two hydrogen atoms, could be detected by this method.

Fischer's independent proof of the position of the phytol group in chlorophyll may now be mentioned. When ethyl chlorophyllide (VIII) is treated with hydrogen iodide, the ethyl ester of pheoporphyrin  $a_5$  is formed. This, on heating, is converted into the ethyl ester of phylloerythrin, which has only one acid group, *viz.*, the propionic acid grouping in position 7. Hence the ethyl group in ethyl chlorophyllide, and therefore also the phytol group in chlorophyll, must be in the propionic acid side chain (66). Stoll's suggestion that since pheophytin is usually prepared with an alcoholic solution an interchange of ester groups may have taken place is not valid for the above argument (84). In any case, Fischer, using pheophytin prepared with acetone in place of alcohol, finds no difference in the results (24).

Many of the chlorophyll porphyrins can be oxidized by iodine, and analysis of the products shows that oxidation has taken place in position 10 (35). For example, pheoporphyrin  $a_5$  (XVI) with iodine in alcohol in the presence of sodium acetate is converted into 10-hydroxypheoporphyrin  $a_5$  (or neopheoporphyrin  $a_5$ ). If sodium carbonate is substituted for the acetate, the product is 10-ethoxypheoporphyrin  $a_5$  (or pheoporphyrin  $a_5$ ; XXII d) (53). A series of homologous ethers has been prepared by the use of the corresponding series of alcohols in this oxidation (55). Pheophorbide  $a$  itself can be oxidized with iodine in glacial acetic acid (53), yielding 10-hydroxypheophorbide  $a$  (XXI). This Fischer considers as further confirmation of his hypothesis that the carbocyclic ring

in the pheophorbides (and hence in chlorophyll) is identical with that of the derived chlorophyll porphyrins such as phylloerythrin.

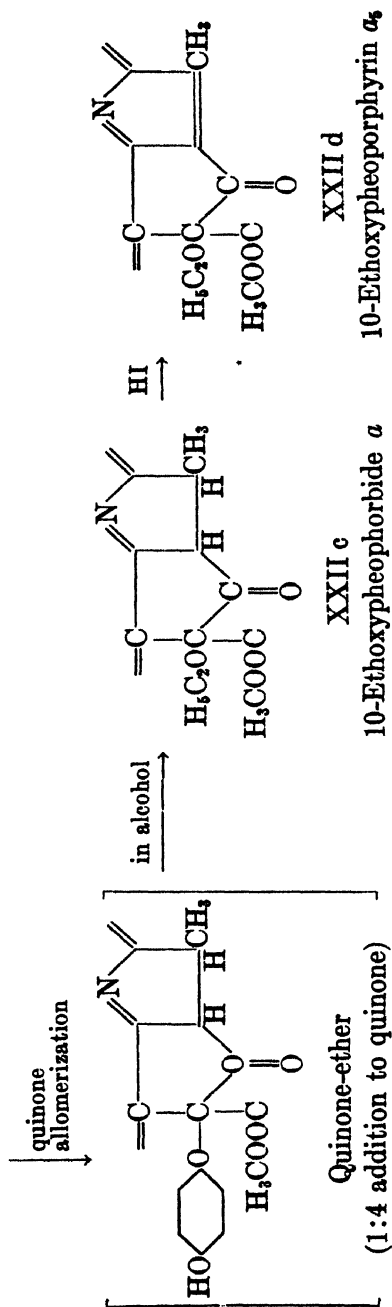
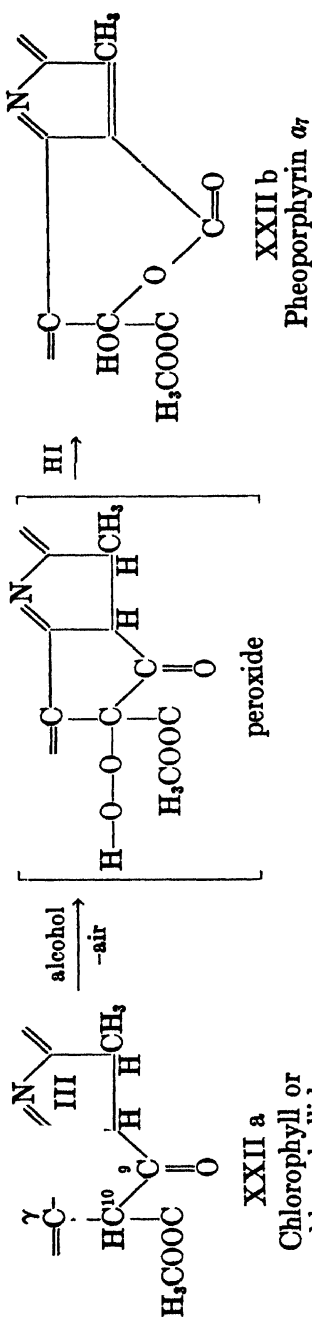


#### *Allomerization and the phase test*

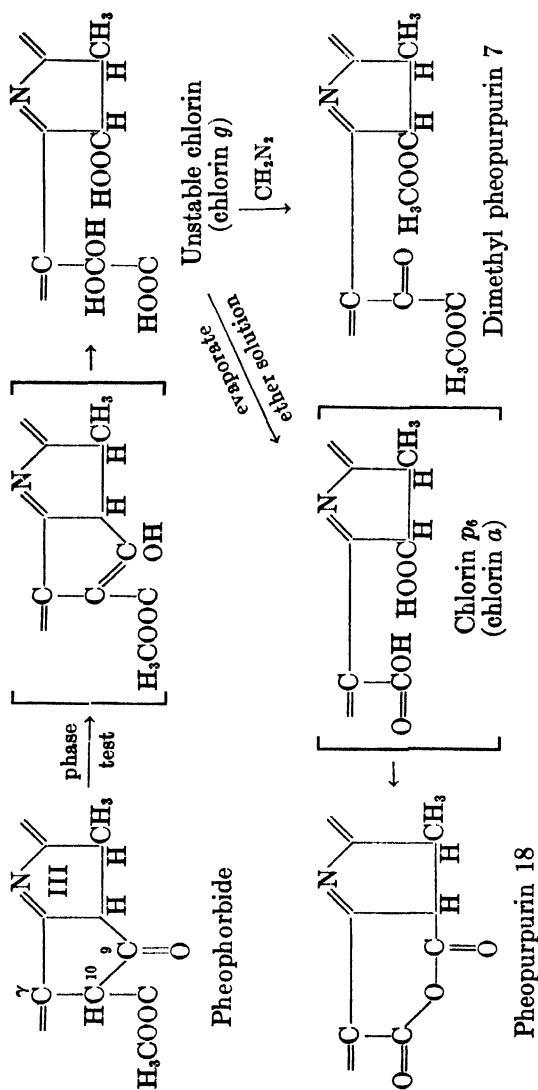
Fischer found that if allomerized chlorophyll (page 11) is treated with hydrogen iodide, followed by hydrolysis with hydrochloric acid, pheoporphyrin  $a_7$  results (66). Similar treatment of chlorophyll itself yields pheoporphyrin  $a_8$  as does pheophorbide  $a$  (XVIII). Now pheoporphyrin  $a_7$  is also obtained from chloroporphyrin  $e_4$  by the iodine-glacial acetic acid oxidation described above, and from the latter relationship formula XXII b has been deduced. On esterification this compound forms a triester, with hydrolysis of the lactone ring. Fischer has abandoned the theory that the first step in allomerization is dehydrogenation between positions 10 and  $\gamma$ , and now suggests peroxide formation; no proof for this has been cited so far. But Conant (5) found that allomerized chlorophyll (allomerized with one mole of oxygen) was apparently identical with dehydrochlorophyll, prepared by oxidation of chlorophyll with two equivalents of oxidizing agent; in other words, the reaction appears to be chlorophyll  $a + O_2 \rightarrow$  dehydrochlorophyll  $a$  (or allomerized chlorophyll) +  $H_2O_2$ . Fischer's peroxide calls for four equivalents. (See page 19.)

Fischer also carried out allomerization experiments in alcohol, using quinone as hydrogen acceptor in place of atmospheric oxygen (66, 28). Treatment of the resulting allomerized chlorophyll with hydrogen iodide gave 10-ethoxypheoporphyrin  $a_8$ . Fischer's latest interpretation of these reactions is given above (63). (The removal of the two hydrogen atoms in nucleus III in the hydrogen iodide reaction will be discussed later.)

With regard to the phase test, Conant insisted that esterification with diazomethane could not accomplish an oxidation of the unstable chlorin, and that the latter must therefore be at the same oxidation level as pheopurpurin 7. Fischer finally agreed with this interpretation. According to Fischer, in the presence of alkali enolization takes place in position 9 with the formation of a double bond between 9 and 10. Then follows





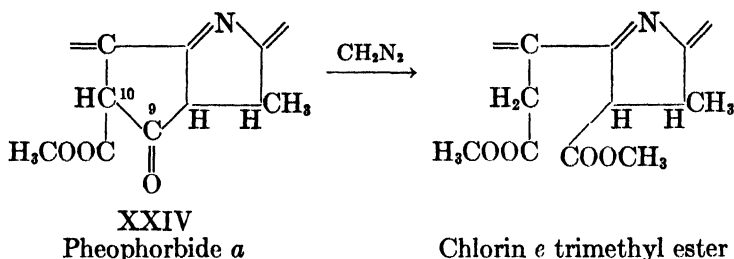


## XXIII

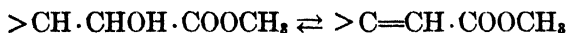
The phase test (Fischer)

rupture of this bond by oxidation, accompanied by hydrolysis of the carbomethoxyl group on 10, and the unstable chlorin is, he suggests, a hydrated keto acid (17). (Conant's monomethyl chlorin *g* (IX) might also be a hydrate.) Immediate esterification converts the unstable chlorin to the trimethyl ester, dimethyl pheopurpurin 7. If an ethereal solution of the unstable chlorin is allowed to stand, or is evaporated to dryness, pheopurpurin 18 results (11). Fischer showed that formic acid was split out in this reaction (32), and suggests (17) that chlorin *p*<sub>8</sub> (*vide infra*) is probably an intermediate product, although it was not isolated in this reaction. (See page 20.)

Conant and Fischer differ in their proposed formulas for chlorin *e* and its triester. Willstätter prepared chlorin *e* by the action of hot alkali on the pheophorbides (VIII), and showed that it formed a triester on esterification. Fischer (32) found that the action of diazomethane in methyl alcohol, or of phosgene and alcohol, was sufficient to convert pheophorbide *a* into chlorin *e* trimethyl ester, and considers that the reaction is a simple methanolysis between carbon atoms 9 and 10.



Similar opening of the pheophorbide carbocyclic ring has been achieved by the use of methylamine and of ammonia, the products being the corresponding acid amides of chlorin *e* ester (substituted in the 6-position) (31). The trimethyl ester of chlorin *e* is, according to Fischer (58), isomeric with the triester of chlorophyllin *e*<sub>8</sub> (XVII); and from calorimetric data (79) these appear to have equal energy values. Fischer concludes that the side chains have the same state of oxidation, *viz.*, a  $\gamma$ -acetic acid side chain, as shown in the formula above. Conant (1), on the other hand, proposed for chlorin *e* a formula containing a potential lactic acid side chain



similar to that in his formula for chlorophyll *a* (XIII). This would explain the identical behavior of chlorin *e* triester and pheophorbide toward the phase test, resulting in the unstable chlorin and the pheopurpurins. That chlorin *e* triester, but not chlorin *e* itself, gives the phase test with

formation of the unstable chlorin, is explained by Fischer as activation of the hydrogen atoms on carbon atom 10 by the carbomethoxyl group in the former case (17); but it is difficult to see why this should admit of the addition of two oxygen atoms in the 10-position, as is required by Fischer's formula for the unstable chlorin. Again, Conant's formula would explain the clear-cut quantitative oxidation of chlorin *e* by molybdcyanide (5) (two equivalents of oxidizing agent being used), analogous to the molybdcyanide oxidation of pheophorbide and chlorophyll. With chlorin *e*, carbon dioxide is evolved, and the product isolated is chlorin *k*, containing a lactone ring (2). This quantitative oxidation would indicate that the state of oxidation of the 10-position in chlorin *e* is  $>\text{CHOH}$ , not  $>\text{CH}_2$ ; and by analogy, it also throws in doubt the state of oxidation of position 10 in Fischer's formula for pheophorbide *a*. This difficulty is entirely separate from any argument for or against the carbocyclic ring. Fischer himself at one time (66) had a hydroxyl group in place of a hydrogen in position 10 of pheophorbide. The other reactions of chlorin *e* and its esters, e.g., the reactions of the diester with hydrogen iodide, by Fischer and Kellerman (41), are as easily explained on Conant's formulation as on Fischer's.

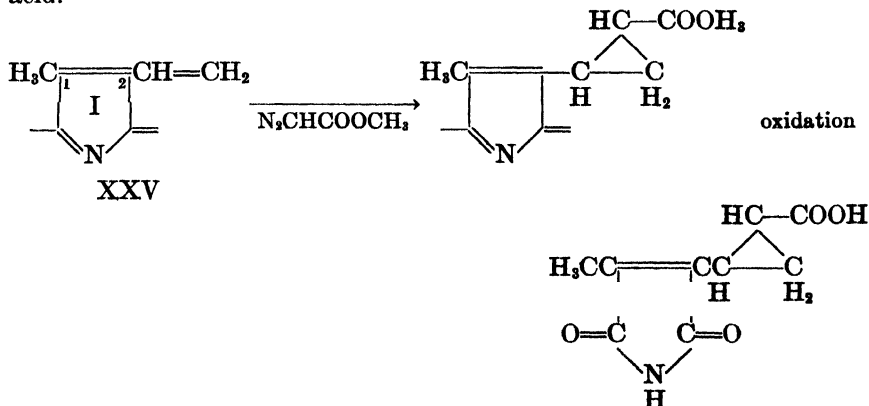
#### *The vinyl group*

At the time Conant proposed his formula for chlorophyll *a* he insisted that the chlorophyll nucleus should be considered to have a dihydroporphyrin structure. Fischer, on the other hand, on the basis of isomerization with hydrogen iodide, contended that chlorophyll was an isomerized porphyrin. These two views became reconciled by the later work of Fischer. Three types of reaction established that chlorophyll, the phorbides, chlorins and purpurins—in fact all the non-porphyrin derivatives (but including isorhodoporphyrin) of chlorophyll *a*—contained an unsaturated side chain. In the first place, if pheophorbide is hydrogenated with addition of three molecules of hydrogen, a leuco compound is formed, which in an acid medium is converted into a porphyrin, *viz.*, pheoporphyrin *a<sub>8</sub>*. If however a neutral medium is employed, or the hydrogenation is stopped on the addition of two moles of hydrogen, dihydropheophorbide *a* is obtained (44). Stoll and Wiedemann also obtained this dihydro reaction (85). Dihydro compounds are also obtainable from chlorin *e* and from purpurin 7; spectroscopically they differ very slightly from the parent substances,—an indication that the unsaturated group involved is not part of the nuclear structure.

Secondly, Fischer found that if his hydrogen iodide reaction was carried out in the cold, instead of at temperatures of 50° or 60°C., a new series of compounds, ketoporphyrins in structure, were obtained (52, 53). For instance, chlorophyll *a* and pheophorbide *a* both yield oxopheoporphyrin

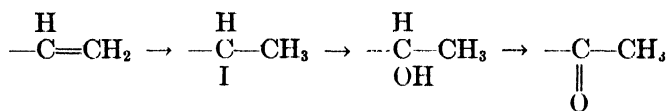
$a_6$ , pyropheophorbide yields oxophylloerythrin, chlorin  $e$  trimethyl ester yields oxochloroporphyrin  $e_6$ , while chlorin  $e$  yields oxochloroporphyrin  $e_6$ . The two former oxo compounds contain two keto groups each. On heating oxophylloerythrin, or on heating oxochloroporphyrin  $e_6$  with sulfuric acid, an oxorhodoporphyrin is formed. Fischer first suggested a methylene group in chlorophyll as giving rise to the oxo reaction (the oxo derivative would then contain a formyl group), then changed it to an ethylidene residue (the oxo derivatives would then possess an acetyl group). That the acetyl residue was the oxo group was shown by the conversion of oxorhodoporphyrin to normal rhodoporphyrin by the Wolff-Kishner reaction ( $-\text{COCH}_3 \rightarrow -\text{CH}_2 \cdot \text{CH}_3$ ). The position of the acetyl residue and therefore also of the parent unsaturated group was established by the fact that oxophylloerythrin heated in a sealed tube with concentrated hydrochloric acid (which replaces the oxo group by hydrogen), followed by esterification, gave a desethylphyloerythrin and a desethylpyrroporphyrin. The latter compound was identical with a synthetic 2-desethylpyrroporphyrin. Also, the desethylphyloerythrin could be reduced to a desethyldesoxophylloerythrin, and the latter was identical with one of the two possible synthetic desethyldesoxophylloerythrins, *viz.*, the 2-desethyl (54). Hence the unsaturated group in the chlorophyll molecule is in the 2-position, and the oxo group must be an acetyl group in order to give rise to a desethyl- and not a desmethylporphyrin.

The third reaction, that of diazoacetic ester, proved conclusively that the unsaturated group was a vinyl residue (46). This too will produce an acetyl group on oxidation. Hemin and one of the blood porphyrins, protoporphyrin, have been shown by synthesis to contain a vinyl group. Diazoacetic ester adds on to this vinyl group with evolution of nitrogen, and on drastic oxidation of the addition compound with chromic acid, one of the products isolated was methyl maleic imide-cyclopropyl carboxylic acid.



The pheophorbides, the chlorins derived from chlorophyll, and the purpurins, but not the porphyrins (except isorhodoporphyrin), add diazoacetic ester in a completely analogous manner. Drastic oxidation of some of these addition products gave the same imide as was obtained from protoporphyrin. The action of hydrogen iodide and of pyrolysis on diazoacetic ester addition products of these chlorophyll derivatives gave diazoacetic ester derivatives of the corresponding compounds. For instance, hydrogen iodide on the derivative of pheophorbide *a* gave the derivative of pheoporphyrin *a*<sub>6</sub>, while pyrolysis of the former gave the diazoacetic ester derivative of pyropheophorbide *a*, identical with that obtained by direct action of diazoacetic ester on pyropheophorbide. In short, the relationships shown on page 14 are also valid for the diazoacetic ester derivatives.

The existence of a vinyl group in position 2 in the molecules of chlorophyll and of its immediate derivatives gives a simple explanation of the oxo reaction. Hydrogen iodide adds on to the vinyl group, hydrolysis occurs with replacement of iodine by the hydroxyl group, and spontaneous dehydrogenation takes place to the acetyl residuc:



## XXVI

The oxo reaction

Since pheoporphyrin *a*<sub>6</sub> is isomeric with pheophorbide *a*<sub>6</sub>, the hydrogen iodide isomerization must be in effect a migration of two hydrogen atoms from somewhere in the nucleus to the vinyl group. The porphyrins which result contain an ethyl residue in the 2-position.

Pheopurpurin 7 gives a diazoacetic ester addition product (64) and also undergoes the oxo reaction; it therefore contains the vinyl group. This group is retained in chlorin *f*, obtained by alkaline hydrolysis of purpurin 7 (XII). Isorhodoporphyrin also contains the vinyl group in contrast to the other chlorophyll porphyrins. It gives addition products with bromine and with diazoacetic ester, and the latter compound is identical with that obtained by the action of boiling pyridine on the diazoacetic ester addition product of purpurin 7 (43).

Again, 10-hydroxypheophorbide *a* (XXI) both shows the diazoacetic ester reaction and undergoes the oxo reaction. The product in the latter case is oxorhodoporphyrin (43), shown to be (2-desethyl)-2-acetyl rhodoporphyrin (i.e., it contains  $-\text{COCH}_3$  in place of  $-\text{C}_2\text{H}_5$  in the 2-position), as follows. The action of bromine replaces the acetyl group by bromine, and the bromo compound can then be debrominated by the use of hydra-

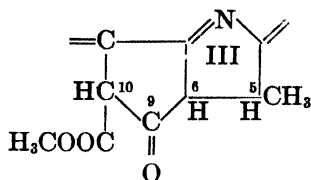
zine hydrate with a catalyst; the resulting 2-desethylrhodoporphyrin had already been synthesized (20). It was also possible to synthesize the acetylrhodoporphyrin; the acetyl group was introduced into 2-desethylrhodoporphyrin by the action of acetic anhydride and stannic bromide on the iron salt (hemin) (43).

The relationship between isorhodoporphyrin and rhodoporphyrin was elucidated by the following reactions. Introduction of the formyl residue (57) into 2-desethylrhodoporphyrin gave a (2-desethyl)-2-formylrhodoporphyrin (43). The action of methylmagnesium iodide on this compound replaces the formyl group with the hydroxyethyl group ( $-\text{CHOH} \cdot \text{CH}_3$ ), and the latter was spectroscopically identical with (2-desvinyl)-2-hydroxyethylisorhodoporphyrin, prepared by the action of hydrogen bromide in acetic acid on isorhodoporphyrin. Again, if isorhodoporphyrin is heated with phenazine, the vinyl group is oxidized to a formyl group, and the product is identical with (2-desethyl)-2-formylrhodoporphyrin. Hence isorhodoporphyrin is a 2-vinylrhodoporphyrin, and is not a true isomer of rhodoporphyrin, since it contains two hydrogen atoms fewer. Confirming this, pheopurpurin 7 (39) on being heated with pyridine gives isorhodoporphyrin, while dihydropheopurpurin 7 gives rhodoporphyrin. Rhodochlorin (Conant's chlorin *f*) with hydrogen iodide gives rhodoporphyrin, but the diazoacetic ester addition product of rhodochlorin gives the corresponding addition product of isorhodoporphyrin. The difference between the two porphyrins is therefore in the vinyl group. A further proof of this relationship is afforded by drastic oxidation with chromic acid. In the blood pigment series it was found that an unsaturated side chain such as the vinyl group caused the complete destruction of the nucleus concerned; if, however, an ethyl group were present, methylethylmaleic imide (II b) was obtained. Similarly in the chlorophyll series, Fischer (24) found that the dihydro compounds yielded double the amount of methylethylmaleic imide that was given by the unhydrogenated compounds, and in particular that rhodoporphyrin gave twice as much imide on oxidation as isorhodoporphyrin. The establishing of the relationship between rhodo- and isorhodo-porphyrins was made more difficult by the attempt to fit the verdoporphyrin of Treibs and Wiedemann into the chlorophyll system. These authors (91) discovered that a large number of the chlorophyll porphyrins isolated by Willstätter were not single compounds but mixtures, and they isolated what they considered to be a new single chlorophyll porphyrin, verdoporphyrin (90). Conant (13) was never able to obtain this compound by any method, but isolated only isorhodoporphyrin. Fischer isolated verdoporphyrin by the method of Treibs, and also obtained it from pheoporphyrin  $a_5$  (27). In the former case the product appears to be a mixture of rhodo- and isorhodo-

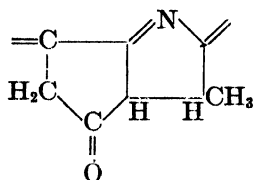
porphyrins, and in the latter a mixture of rhodoporphyrin and chloroporphyrin *e*<sub>8</sub>, according to recent findings of Fischer (40).

*Optical activity and the dihydroporphin nucleus*

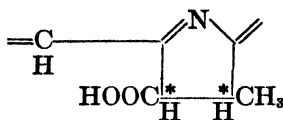
Stoll and Wiedemann (88), using monochromatic light, found that chlorophyll, pheophytin, and pheophorbide were optically active. Fischer and Stern (63) used white light, whereby higher concentrations of substance could be employed, and found that not only chlorophyll and the phorbides, but also the chlorins and purpurins were optically active. Pyropheophorbide, prepared either from pheophorbide or by ring closure of chlorin *e* (XVIII), showed the same specific rotatory power. Now the carbocyclic ring of pheophorbide contains an asymmetric carbon atom in position 10, but in pyropheophorbide this asymmetry is no longer present. Hence there must be at least one other asymmetric center. Fischer therefore suggested that the two surplus hydrogen atoms in the chlorophyll nucleus which convert the vinyl group to ethyl in the hydrogen iodide isomerization to the porphyrin nucleus be placed one on the  $\gamma$ -carbon atom, and one on a nitrogen atom in one of the pyrrole rings. The  $\gamma$ -carbon atom would then be asymmetric; pyropheophorbide could be optically active, but conversion to phylloerythrin would destroy this asymmetry. Phylloerythrin (formula XV) was in fact found to be optically inactive. The decisive argument against asymmetry in the  $\gamma$ -position was that rhodochlorin (Conant's chlorin *f*; formula X), which has no substituents in the  $\gamma$ -position, is still optically active. Hence there must be at least one asymmetric center somewhere else than in positions 10 and  $\gamma$  in the chlorophyll molecule. Fischer therefore then placed the two surplus hydrogen atoms of the dihydroporphin nucleus of chlorophyll, the phorbides, and the chlorins and purpurins, in positions 5 and 6 of nucleus III, thus forming a dihydropyrrole nucleus (50).



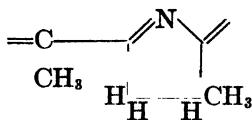
XXVII a  
Pheophorbide



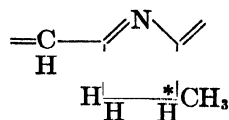
XXVII b  
Pyropheophorbide



XXVIII a  
Rhodochlorin (Fischer)

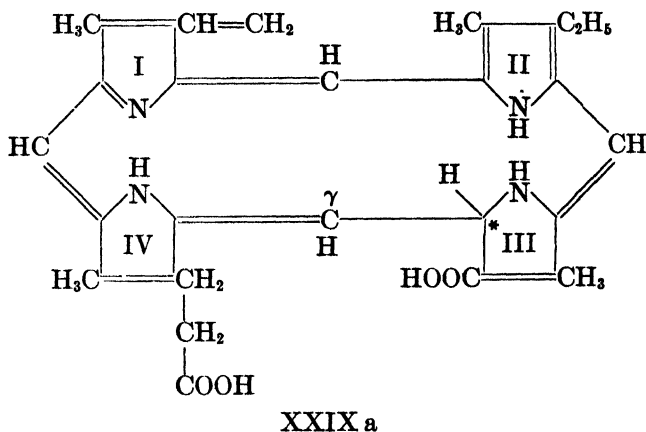


XXVIII b  
Phyllochlorin

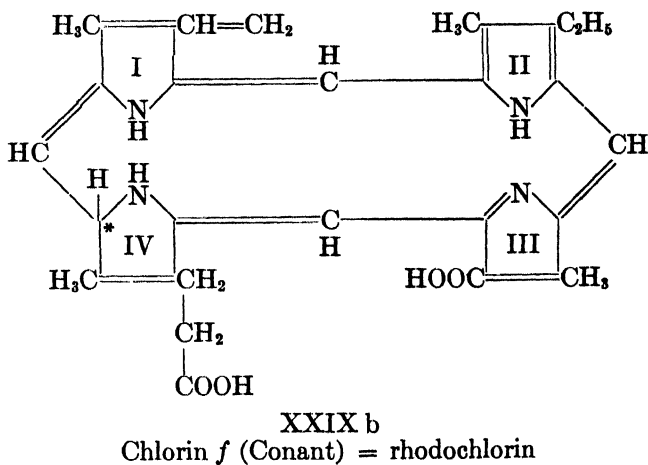


XXVIII c  
Pyrrochlorin

Conant (3) had previously made a similar suggestion on the basis of titration results on the basicity of chlorophyll derivatives (*vide infra*). These results indicated that the porphobides and the chlorins contained a nucleus of basicity comparable to the amide  $R-NH-COR$ , and this nucleus was either III or IV, since only these two carried acidic groups. The following formulas indicate Conant's suggestions for the possible structure of chlorin *f* (the vinyl group proved by Fischer has been incorporated). Both formulas contain one asymmetric carbon atom, marked by asterisks.



or

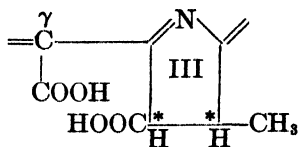


Fischer found that another simple chlorin, phytylchlorin (Conant's pyrochlorin *e*, obtained by pyrolysis of chlorin *e* (8)) is also optically active

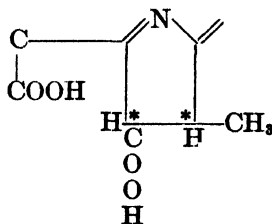


(41). It differs from rhodochlorin in that it contains a methyl group on the  $\gamma$ -carbon atom, and no carboxyl group in the 6-position (*cf.* the difference between rhodo- and phyllo-porphyrins). Pyrrochlorin, with no substituents in either the  $\gamma$ - or the 6-position, has been prepared by the decarboxylation of rhodochlorin (39); it also is optically active. Fischer's formulas for these three chlorins are given above (XXVIII); the asymmetric centers are indicated by asterisks. The formulas for phyllo- and pyrro-chlorins derivable from either of Conant's formulas for chlorin *f* would also retain the asymmetric center. Hence the optical activity of these three chlorins does not determine the position of the two "extra hydrogens."

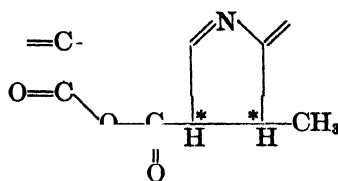
In Fischer's formula for rhodochlorin there are two asymmetric carbon atoms, therefore theoretically two racemic and four optically active modifications are possible. Fischer claims to have found this type of isomerism in compounds closely related to rhodochlorin (40). Conant (11) showed that pheopurpurin 18 (an anhydride; figure XXIII) on alkaline hydrolysis yielded the tribasic acid, chlorin *a*, which formed a trimethyl ester on treatment with diazomethane. Fischer (32) called the new substance chlorin *p*<sub>6</sub>, and established its structure as that of a rhodoporphyrin- $\gamma$ -carboxylic acid, except that it contains the vinyl group and the two extra nuclear hydrogen atoms. It is a dextrorotatory substance. Fischer also obtained a compound apparently isomeric with chlorin *p*<sub>6</sub> by the action of dilute sodium hydroxide in the presence of air on pheophorbide *a*. The new compound, pseudochlorin *p*<sub>6</sub>, differs from chlorin *p*<sub>6</sub> spectroscopically, and in optical activity; it is levorotatory. They are not, however, optical antipodes. Similarly the dihydro derivatives (40) and the diazoacetic ester addition products of the two chlorins differ in spectrum and in optical activity. The chlorins also differ in chemical activity. Chlorin *p*<sub>6</sub> and its dihydro compound revert spontaneously to pheopurpurin 18 and its dihydro compound, respectively, while pseudochlorin *p*<sub>6</sub> only gives pheopurpurin 18 on heating, and the dihydro compound is completely stable. Fischer's explanation is that the carboxyl groups in the normal series are adjacent to each other, and thus anhydride formation is possible (formulas XXX).



XXX a  
Chlorin *p*<sub>6</sub>

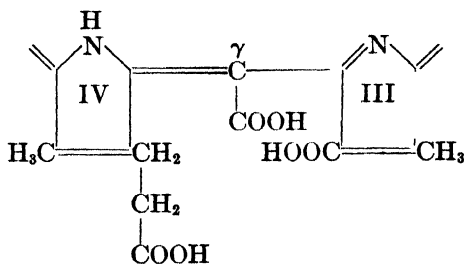


XXX b  
Pseudochlorin *p*<sub>6</sub>



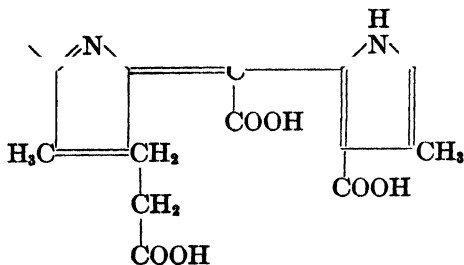
XXX c  
Pheopurpurin 18

Further, chlorin  $p_6$  with hydrogen iodide gives rhodoporphyrin- $\gamma$ -carboxylic acid, which with concentrated sulfuric acid forms a green anhydride. Pseudochlorin  $p_6$  with hydrogen iodide gives a rhodoporphyrin- $\gamma$ -carboxylic acid which differs in mixed melting point and spectrum, and is decomposed by sulfuric acid. A similar result is obtained when the diazoacetic ester addition products of the two chlorins are used. Since there cannot be optical isomerism dependent on position 6 in rhodoporphyrin- $\gamma$ -carboxylic acid, Fischer assumes that the form which gives no anhydride must have undergone isomerization in the hydrogen iodide treatment, with rearrangement of hydrogen atoms in all the pyrrole nuclei (XXXI). So far, no investigator has ever shown the existence of two such isomers of one compound in the chlorophyll series, especially in the porphyrins (which have been exhaustively investigated for such isomers).



XXXI a

Rhodoporphyrin- $\gamma$ -carboxylic acid from chlorin  $p_6$ ; forms anhydride



XXXI b

Rhodoporphyrin- $\gamma$ -carboxylic acid from pseudochlorin  $p_6$ ;  
forms no anhydride

If the two chlorins had given the same rhodoporphyrin- $\gamma$ -carboxylic acid, the evidence for an asymmetric center at position 6 would have been conclusive. But the postulation of this new rhodoporphyrin acid throws doubt on the whole question of the relation between chlorin  $p_6$  and pseudochlorin  $p_6$ .<sup>2</sup>

*The exact structure of the chlorophyll molecule*

Adopting the method of Tschugaeff and Zerewitinoff (92), in which active hydrogen atoms are measured by their reaction with methylmagnesium iodide, and later the modified method of Schmitz-Dumont and Hamon (74), Fischer in a series of papers estimated the active hydrogen atoms in chlorophyll derivatives. In the simple esterified porphyrins, e.g., rhodoporphyrin dimethyl ester, two active hydrogens were found; these appeared to be the hydrogens in two imino groups, corresponding to formula Va. Methyl pheophorbide *a* and pheoporphyrin *a*<sub>2</sub> dimethyl ester contain a third active hydrogen (30), and this is the labile hydrogen in position 10, which in the former case is responsible for enol formation in the phase test. The presence of the carbomethoxyl group in position 10 appears to influence the lability of the hydrogen atom, for pyropheophorbide *a* (XXVII b) shows only two active hydrogen atoms, and does not give the phase test reaction. But a hydroxyl group in position 10 of pheophorbide *a* would also give these results. Isorhodoporphyrin (2-vinyl-rhodoporphyrin) shows anomalous results, having apparently only one active hydrogen atom.

The actual arrangement of the double bonds in the chlorophyll molecule appears to be no longer entirely arbitrary. Fischer, Stern, and co-workers examined spectroscopically most of the chlorophyll derivatives, and established certain general laws (80). If a porphyrin contains a carbonyl group in a nucleus, the spectrum is closely related to that of rhodoporphyrin. If the porphyrin contains two carbonyl groups, then two types of spectra are possible. The "rhodo" type appears if one carbonyl is on a nucleus and the second carbonyl is in the  $\gamma$ -position, or

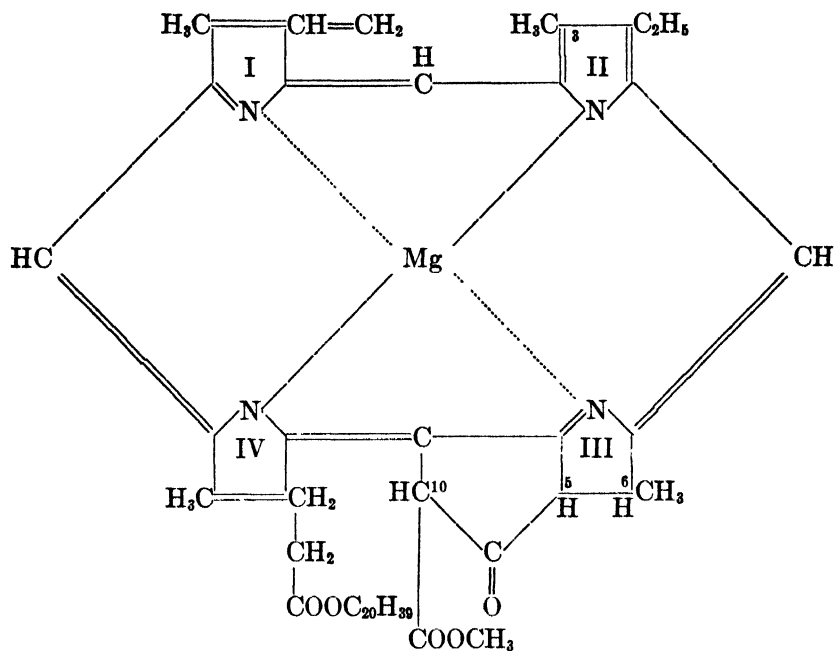
<sup>2</sup> The latter is formed in a reaction which is very closely related to the phase test. This preparation differs from the preparation of monomethylchlorin *g* chiefly in temperature (50°C. compared with 0°C.) and in time (ten hours compared with from 30 minutes to one hour). This suggests that the  $\gamma$ -carbon atom in pseudochlorin  $p_6$  may carry a potential glyoxalic acid side chain; such a compound (an isomer of the unstable chlorins or of monomethylchlorin *g*) could give pheopurpurin 18 on being heated, and with hydrogen iodide might give a rhodoporphyrin- $\gamma$ -glyoxalic acid, which would naturally form no anhydride with sulfuric acid, but would be decomposed. Against this argument are the analyses, and the fact that pseudochlorin  $p_6$  does not give dimethylpheopurpurin 7 on esterification.

between the  $\gamma$ - and  $\delta$ -positions in a carbocyclic ring in conjugation with the whole porphin nucleus; or again, if the two carbonyl groups are situated in alternate pyrrole nuclei, e.g., I and III, or II and IV. On the other hand, if the two carbonyl groups are in adjacent nuclei, or not in conjugation with the porphin system, then the "rhodo" type spectrum is absent. Applying this generalization, it can be shown that nucleus IV has a pyrrole structure and nucleus III a pyrrolenine structure, and that the double bond at the  $\gamma$ -carbon atom is attached to IV and not to III. Briefly, chlorophyllin *a*, dimethyl ester is a  $\gamma$ -formylrhodoporphyrin dimethyl ester, but it does not show a "rhodo" type spectrum; similarly the trimethyl ester of rhodoporphyrin- $\gamma$ -carboxylic acid has a spectrum different from the "rhodo" type, hence the double bond of the carbon atom cannot be attached to nucleus III. The position of the double bond between the  $\gamma$ -carbon atom and nucleus IV was suggested earlier by Fischer (64), as he found that models constructed with the double bond to nucleus III showed a much larger amount of strain. How far these results apply to the chlorophyll molecule itself is still an open question. Conant and Kamerling's spectroscopic data (9) at low temperatures indicate that in chlorophyll and its non-porphyrin derivatives there is a break in the conjugated system of the porphyrins. Conant's formula for chlorin *f* (XXIX) takes this into account; Fischer's formulas (*cf.* XXVIII *a* and XXXII) do not.

Conant (3) attempted to establish the types of nuclei present in the chlorophyll molecule by potentiometric titrations in glacial acetic acid with perchloric acid. Comparing chlorophyll derivatives with simple nitrogenous compounds containing the pyrrole, isopyrrole (or maleic imide), and pyrrolenine (tertiary nitrogen as in pyridine) structures, he found that porphyrins showed two strongly basic groups comparable to two pyrrolenine nuclei (*cf.* nuclei I and III in formula III). The chlorins, on the other hand, had only one strongly basic group (nucleus I in formula XXIX *a* or nucleus III in formula XXIX *b*), and one group intermediate in basicity between a pyrrolenine and a pyrrole structure (nucleus III or IV, respectively). To accommodate these findings, Conant suggested the hydrogenated pyrrolenine nucleus shown (formula XXIX). In general, therefore, Conant's results agree with those of Stern, and in particular corroborate the fact that in the chlorins, and therefore in chlorophyll, it is a pyrrolenine nucleus of the porphyrins which carries the two hydrogen atoms to form the dihydroporphin nucleus. On the other hand, the basicity of this hydrogenated nucleus is comparable to  $R-NH-COR$ , and is less basic than Fischer's nucleus III would be.

The following formula for chlorophyll *a* is the most recent of those sug-

gested by Fischer, on the basis of the results summarized in the previous pages:

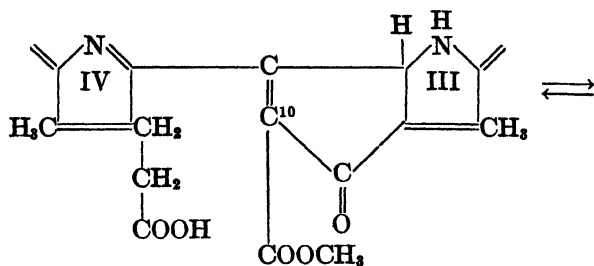


XXXII  
Chlorophyll *a* (Fischer, 1936)

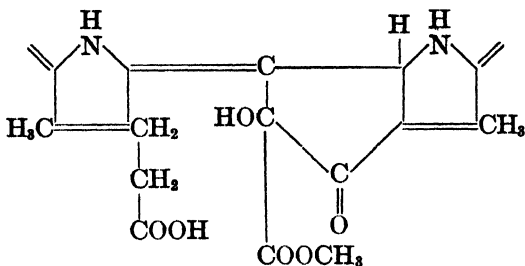
Since a paper by Dr. Fischer summarizing his views follows this review, it will perhaps not seem too critical of his brilliant work if the objections to this present formula—many of them have already been indicated—are summarized:

(a) The position of the hydrogen atoms in positions 5 and 6 needs further proof than the apparent isomerism between chlorin *p*<sub>6</sub> and pseudochlorin *p*<sub>6</sub>.

(b) The state of oxidation of carbon atom 10 in chlorin *e* and therefore also in pheophorbide *a* appears open to question. In the former case, the experimental data indicate a >CHOH grouping in position 10. How such a grouping could be interpolated in the pheophorbide *a* formula and still explain all the results is more difficult. An unsaturated carbocyclic ring may be the answer; for instance, the following formula for pheophorbide derived from formula XXIX *a* for chlorin *f* and incorporating the carbocyclic ring is one possibility.



XXXIII a  
Pheophorbide



XXXIII b  
(1,4-addition of H<sub>2</sub>O)

An interesting point in favor of some such unsaturation at position 10 is Fischer's finding that pheophorphyrin *a*<sub>8</sub> is optically inactive (64), although it contains an asymmetric center in position 10. Either the carbocyclic ring is affected by the hydrogen iodide treatment, and is therefore *not* the same in pheophorbide and pheophorphyrin *a*<sub>8</sub>, or else a racemic mixture of the two forms, whose optical activity depends on this center of asymmetry, is present in pheophorbide. The latter supposition is hardly tenable.

Removal of the two "extra" hydrogen atoms from nucleus III in formula XXXIII a above, might lead to 1,4-addition in position 10 and on the nitrogen of this nucleus. Fischer (45) found that the two hydrogen atoms could be removed by oxidation with silver acetate, and the product was not 2-vinylpheophorphyrin *a*<sub>8</sub>, but 10-acetoxy-2-vinylpheophorphyrin *a*<sub>8</sub>. This fits the above formula equally as well as being explicable by Fischer's theory of activation of the hydrogen on carbon atom 10 by the carbomethoxyl group. The reaction was, however, quantitative after five minutes heating, according to the equation,



This corroborates Fischer's formula as far as it goes, but the experimental details indicate that oxidation, or at least decomposition, continued on longer treatment with excess reagent.

(c) The extreme ease of formation of the carbocyclic ring, shown by Fischer to occur in various syntheses, throws doubt on the proofs of the presence of this ring in pheophorbide and in chlorophyll. The methods of degradation of these compounds to substances which have been shown by synthesis to contain this ring are at least as drastic as the methods of ring closure. Complete proof of the carbocyclic ring could probably only be afforded by the synthesis of pheophorbide.

#### IV. CHLOROPHYLL *b*

Chlorophyll *b* presented a more difficult problem than chlorophyll *a*, chiefly because the yields were very low, and the products much more difficult to purify. It appeared, however, that chlorophyll *b* differed from *a* in that it contained an additional oxygen atom. Willstätter (98) established this by analysis, and various suggestions as to the position of this oxygen atom were advanced. Conant (6), by pyrolysis, phase test reaction, and saponification, obtained from methyl pheophorbide *b* a series of compounds entirely parallel to those in the *a* series (XI). These rhodins, corresponding to the chlorins in the *a* series, still retained the extra oxygen atom, and formed semicarbazones, indicating the presence of a carbonyl group. That this group was in some other part of the molecule than the reactive grouping responsible for the phase test was indicated by the ability of rhodin *l*, the simple rhodin corresponding to chlorin *f* of the *a* series, and which contained no substituent on the  $\gamma$ -bridge carbon atom, to form a semicarbazone. To account for the marked difference in absorption spectrum between the *a* and *b* series, Conant placed this carbonyl group in the nucleus. He replaced a methylene bridge grouping by a  $>\text{C}=\text{O}$  bridge in one of positions  $\alpha$ ,  $\beta$ , or  $\delta$ , but not in  $\gamma$ , because of the properties of rhodin *l*. Warburg (93, 94) also obtained carbonyl derivatives in the *b* series.

Fischer (38), using the hydrogen iodide reaction, showed that pheophorbide *b* and rhodin *g* (analogous to chlorin *e*) gave rise to porphyrins, viz., the pheoporphyrin *b* series and the rhodoporphyrin *g* series, corresponding to the pheoporphyrin *a* and chloroporphyrin *e* compounds of the *a* series (XVIII). Thus he established that pheophorbide *b* contained the carbocyclic ring of the *a* series. He showed that pheophorbide *b* could form an acetal, and also an oxynitrile derivative, while the carbonyl group in the carbocyclic ring is incapable of such reactions. Further, he found that rhodin *g*, in which the carbocyclic ring is no longer present, can still form an oxime with hydroxylamine, indicating that the new carbonyl

group was in some other part of the molecule (25, 38). Since oxidation results on *b* compounds at that time gave no hematinic acid (II a), which is derived from nucleus IV, Fischer originally placed this carbonyl group in the  $\beta$ -position of the propionic acid side chain (26). Meanwhile Stoll and Wiedemann placed the new carbonyl group in the side chain on the  $\gamma$ -bridge as an  $\alpha$ -keto acid (86), and later isolated a dioxime of pheophorbide *b* (89).

Fischer's later work definitely placed the carbonyl group in nucleus II of chlorophyll *b*. The action of hydrogen iodide on the trimethyl ester of rhodin *g* gives the trimethyl ester of rhodoporphyrin *g*<sub>7</sub> (corresponding to chloroporphyrin *e*<sub>8</sub>, formula XVII). This compound forms a mono-oxime, indicating that it still contains the carbonyl group of the *b* series. It gives the oxo reaction, with the formation of rhodoporphyrin *g*<sub>8</sub>, which can no longer form an oxime, and which has acquired an additional carboxyl group, indicating that the parent compound had a formyl group (21). Hydrogen bromide or hydrogen chloride at high temperatures gave rise to 3-desmethylphyllporphyrin and 3-desmethylpyrroporphyrin, hence the formyl group in the *b* series is in the 3-position, replacing a methyl group of the *a* series (21, 84). Final and definite proof was given by the synthesis of 3-desmethyldesoxophylloerythrin (cf. formula XIV). This compound is obtainable from the ester of rhodoporphyrin *g*<sub>8</sub> by reduction, whereby the 3-carboxyl group is reduced to a hydrogen atom, and ring closure is effected between the  $\gamma$ - and 6-positions. Alternately, pyrolysis of rhodoporphyrin *g*<sub>8</sub> in pyridine effects ring closure with formation of pheoporphyrin *b*<sub>7</sub> (cf. *e*<sub>8</sub> to *a*<sub>5</sub>; in the *b* series there is an additional carboxyl group originating from the formyl group). If the oxime (on the carbocyclic carbonyl group) of *b*<sub>7</sub> is heated with hydrogen bromide, it loses two carboxyl groups, and 3-desmethyldesoxophylloerythrin (cf. formula XIV) again results (23). This compound was synthesized (54), and proved the position of a formyl group in the 3-position of chlorophyll *b*.

Chlorophyll *b* and the rhodins contain the vinyl group in the 2-position; diazoacetic ester gives addition products, and that the reaction does not affect the formyl group is proved by the ability of the oximes to form diazoacetic ester addition products (22). The poor yields obtained in the *b* series are due to the presence of the two unsaturated groupings. Fischer showed that if these groups are prevented from reacting, side reactions are eliminated, and the yields parallel and even better those in the *a* series. For instance, pyrolysis of rhodin *g* trimethyl ester gives pyropheophorbide *b* in 10 per cent yield; pyrolysis of the oxime gives a yield of 30 per cent oxime; while pyrolysis of the diazoacetic ester addition product of the oxime gives a 60 per cent yield of the corresponding derivative of pyropheophorbide *b* (17).



It is possible to convert the *b* into the *a* series by converting the formyl group into the methyl group; this was accomplished by catalytic reduction in formic acid of pheoporphyrin *b*<sub>6</sub>, the products being pheoporphyrin *a*<sub>6</sub> and its reduction product, 9-hydroxydesoxopheoporphyrin *a*<sub>6</sub> (33). Fischer's formula for chlorophyll *b* is therefore identical with that of *a* (XXXII), except for the replacing of the methyl group in the 3-position by a formyl group.

## V. ATTEMPTS AT THE SYNTHESIS OF CHLOROPHYLL

For a total synthesis of chlorophyll, the starting material would naturally be phylloerythrin, which has been prepared synthetically. The first step would then be the introduction of the carbomethoxyl residue into the isocyclic ring to give pheoporphyrin *a*<sub>6</sub>. Fischer could not achieve this, although he found it possible to introduce the ethoxyl residue by the iodine oxidation method, with the formation of 10-ethoxyphylloerythrin (53). Higher homologues were also prepared (55). However a partial synthesis of pheoporphyrin *a*<sub>6</sub> was arrived at by ring closure of the 6-formyl derivative of isochlorophyllin *e*<sub>4</sub> ester (XX), which already contains the carbomethoxyl residue, to give 9-hydroxydesoxopheoporphyrin *a*<sub>6</sub> (42). Oxidation of the latter with chromic acid gives pheoporphyrin *a*<sub>6</sub> itself.

Willstätter (9b) introduced the phytol group into pheophorbide biologically by reversing the action of the chlorophyllase enzyme. By the use of phosgene, whereby an acid chloride appears to be formed as an intermediate product, Fischer (56) found it possible to esterify pheophorbide *a* with various alcohols of high molecular weight; these included phytol, geraniol, menthol, cetyl alcohol, and others. Thus a synthesis of pheophytin from pheophorbide was achieved, and the synthetic product was in all its properties identical with natural pheophytin.

Willstätter (97) achieved a synthesis of chlorophyll from pheophytin by introducing magnesium through the medium of the Grignard reagent. Fischer (60) found that in this reaction the phytol group is partially saponified. However he succeeded in introducing magnesium by the Grignard reaction into methyl pheophorbide *a*, with the formation of chlorophyllide *a*, whose identity was established by the hydrogen iodide and allomerization reactions, giving rise to pheoporphyrin *a*<sub>6</sub> ester and its 10-ethoxy derivative, respectively. Fischer (31) later found better conditions for the Grignard reaction, and introduced magnesium into the pheophytin molecule, giving chlorophyll *a* itself, and into pheoporphyrin *a*<sub>6</sub>, giving pheoporphyrin *a*<sub>6</sub>-phyllin.

Similarly in the *b* series, ethyl chlorophyllide *b* was synthesized from ethyl pheophorbide *b* by the use of the Grignard reagent (61).

The question of color in chlorophyll and its derivatives is of interest. Early striking examples were the acid and anhydride pairs; rhodoporphyrin- $\gamma$ -carboxylic acid (XXXI a) is red and its anhydride is green, while pheopurpurin 18 (an anhydride) (XXX c) is purplish-red, and the corresponding acid, chlorin *a* (Conant) or chlorin *p<sub>a</sub>* (Fischer, XXX a), is green. In many cases the difference is merely that of two nuclear hydrogen atoms, as in the simple chlorins, rhodo- (Conant's chlorin *f*), phyllo-, and pyrro-chlorins (XXVIII a, b, and c), compared with the corresponding porphyrins, all of which are red. The difference between the chlorins and the rhodins (red) is in the formyl group. Fischer considers that any oxygen-containing side chain attached to the nucleus will effect this color change, and cites the pheopurpurins, whose colour is analogous to that of the rhodins, and which possess keto groups attached to the  $\gamma$ -carbon atom.

Fischer proposes modifying the nomenclature of the types of chlorophyll derivatives (39); he suggests that they be classified into phorbins, chlorins, and porphins. Phorbins possess the dihydroporphin nucleus and the carbocyclic ring. When this ring is opened, chlorins result; this group therefore includes the rhodins and the purpurins. The prefix "meso" before the phorbins and chlorins indicates an ethyl in place of a vinyl group; i.e., the meso compounds are the former dihydro compounds.

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# CHLOROPHYLL<sup>1</sup>

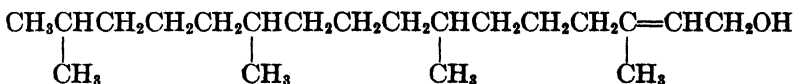
HANS FISCHER

*Technische Hochschule, Munich, Germany*

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The pigment of green leaves is a complex compound of waxy character, consisting of a magnesium-containing pyrrole component and of the alcohols, phytol,  $C_{20}H_{40}O$ , and methyl alcohol, which are esterified to two carboxyl groups of chlorophyll, as we know from the investigations of Willstätter and his coworkers (71).

The constitution of phytol has in the meantime been fully elucidated and proved by synthesis to be as follows (29):



Chlorophyllase, discovered by Willstätter, in an alcoholic medium brings about the replacement of phytol by the alcohol employed, and thus the crystalline methyl- or ethyl-chlorophyllides are obtainable, which prove to be mixtures, like chlorophyll itself. The latter consists of two components, *a* and *b*, of which the *b* component is separable only with difficulty and was very recently obtained pure for the first time by Winterstein and Stein (76, 77) by the chromatographic method; and ethylchlorophyllide *b* was obtained by us (50) by a method of partial synthesis. The latter method is also by far the most convenient for obtaining ethylchlorophyllide *a*. The chlorophyllides possess the following composition (73):

Methylchlorophyllide <i>a</i>	$[C_{32}H_{30}ON_4Mg](COOCH_3)_2 + 1/2 H_2O$
Ethylchlorophyllide <i>a</i>	$[C_{32}H_{30}ON_4Mg](COOC_2H_5)(COOCH_3)$
Methylchlorophyllide <i>b</i>	$[C_{32}H_{28}O_2N_4Mg](COOCH_3)_2 + 1/2 H_2O$
Ethylchlorophyllide <i>b</i>	$[C_{32}H_{28}O_2N_4Mg](COOC_2H_5)(COOCH_3)$

By treatment with acids, there is obtained from chlorophyll the magnesium-free pheophytin, which may also be separated into the components *a* and *b*. Under the action of hydrochloric acid or of hydrochloric acid and methyl alcohol, pheophytin gives the pheophorbides, methylpheo-

<sup>1</sup> A paper delivered at the Tercentenary Conference of Arts and Sciences at Harvard University, September, 1936.

phorbide  $a + b$ . Both crystallize extremely well;  $a$  is obtainable pure with relative ease, even in large amounts by employing Dr. Neumann's extraction apparatus, while  $b$  is more difficult to obtain pure. These compounds have the following formulas (74):

Pheophorbide $a$	$[\text{C}_{32}\text{H}_{32}\text{ON}_4](\text{COOCH}_3)(\text{COOH})$
Methylpheophorbide $a$	$[\text{C}_{32}\text{H}_{32}\text{ON}_4](\text{COOCH}_3)_2$
Pheophorbide $b$	$[\text{C}_{32}\text{H}_{30}\text{O}_2\text{N}_4](\text{COOCH}_3)(\text{COOH})$
Methylpheophorbide $b$	$[\text{C}_{32}\text{H}_{30}\text{O}_2\text{N}_4](\text{COOCH}_3)_2$

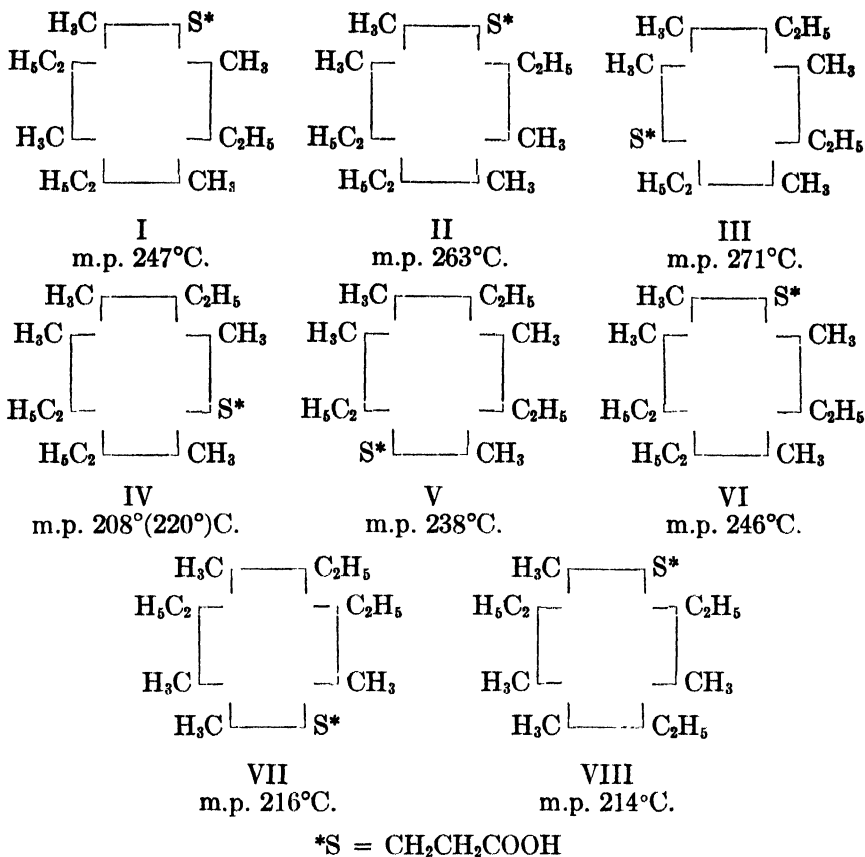
If pheophytin or pheophorbide is subjected to a quick (30 sec.) saponification with methyl alcoholic potassium hydroxide, phytochlorin  $e$  and phytorhodin  $g$  are produced, more briefly designated as chlorin  $e$  and rhodin  $g$ . Chlorin  $e$  corresponds to the  $a$  component, rhodin  $g$  to the  $b$  component. Chlorin  $e$  was observed by Willstätter (75) as occurring in two modifications, as a lactam hydrate of the formula  $\text{C}_{34}\text{H}_{36}\text{O}_6\text{N}_4$  and as a lactam  $\text{C}_{34}\text{H}_{34}\text{O}_6\text{N}_4$ . In the theoretical introduction to his book on chlorophyll, only the latter formula is given on page 15.

Phytorhodin  $g$  (72) possesses the composition  $\text{C}_{34}\text{H}_{32}\text{O}_7\text{N}_4$ . Phytochlorin  $e$  was regarded as a tricarboxylic acid with two carboxyl groups free and one bound as a lactam. Phytorhodin  $g$  was considered a tetracarboxylic acid (72), with only two or three carboxyl groups free.

Chlorin  $e$  gives a beautifully crystalline trimethyl ester which, according to Treibs and Wiedemann (69), can be prepared with particular ease by means of diazomethane, and possesses the formula  $\text{C}_{37}\text{H}_{42}\text{O}_6\text{N}_4$ . Phytorhodin  $g$  also gives with diazomethane a beautifully crystalline trimethyl ester, of the formula  $\text{C}_{37}\text{H}_{40}\text{O}_7\text{N}_4$ .

By energetic degradation of chlorophyll and its derivatives Willstätter and his coworkers obtained numerous phyllins and porphyrins, notable among which are phyllo-, pyrro-, and rhodo-porphyrin, and the etioporphyrin obtainable from them by pyrolysis, which has been held to be identical with the parent substance of hemin.

It was naturally a matter of outstanding interest to elucidate the structure of these porphyrins, and since in the meantime we had achieved general methods of porphyrin synthesis, there was thus a prospect of clarifying the constitution of the chlorophyll porphyrins by synthesis. Rhodoporphyrin is a dicarboxylic acid; phyllo- and pyrro-porphyrins are monocarboxylic acids, which were held to be isomers by the earlier workers. It seemed most probable to regard them as tetramethyltriethylmonopropionic acid porphins, of which the theory predicts the following eight isomers, henceforth designated as monocarboxylic acids:



The internal structure of the porphin ring is omitted and each of the four pyrrole nuclei is given by a bracket, as in this review only the positions of the substituents will be interchanged.

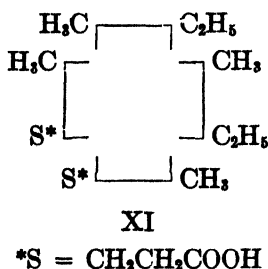
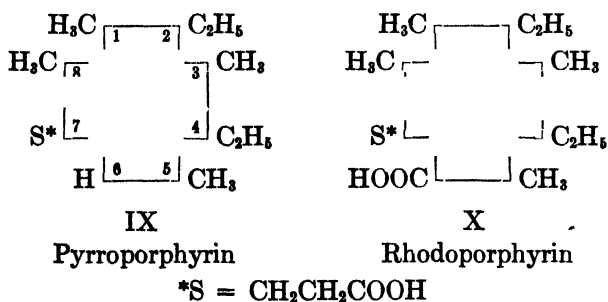
These eight isomers were synthesized (13, 56) and all proved to be different from phyllo- and pyrro-porphyrin.

By analytical methods the presence of a free  $\beta$ -methine group in the latter porphyrins could then be demonstrated, which was lacking in rhodoporphyrin, but was still present in etioporphyrin from chlorophyll. The free methine group in the porphyrins named was demonstrated by bromination and oxidation; a bromine atom entered as a substituent into the porphins, and oxidation gave bromocitraconimide. Hence the most probable view concerning constitution was that the porphyrins mentioned were derived from the monocarboxylic acids by removal of an ethyl group. As this might occur in three ways, theory predicts twenty-four isomeric



pyrroporphyrins and the same number of rhodoporphyrins, since it was highly probable, through the transition from rhodoporphyrin to pyrroporphyrin with splitting off of carbon dioxide, that in place of the free methine group in pyrroporphyrin a nuclear carboxyl group was present in rhodoporphyrin. The synthesis of certain pyrro- and rhodo-porphyrins completely confirmed this assumption (46, 6, 5, 47).

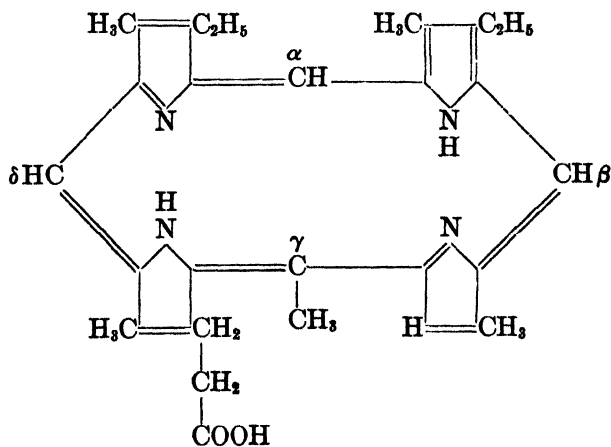
The problem of the constitution of pyrroporphyrin was solved by transforming it into the monocarboxylic acid III by introduction of an ethyl group (2). As this is derived from etioporphyrin III, the fundamental correspondence in the grouping of the side chains in blood and leaf pigment was demonstrated. Both are derivatives of etioporphyrin III. The constitution of pyrroporphyrin, however, was not yet fixed, as the free methine group might be located in the 2-, 4-, or 6-position, all three of which would give the monocarboxylic acid III on introduction of an ethyl group. The 6-position was proved through the synthesis of 1,3,5,8-tetramethyl-2,4-diethylporphin-6-carboxylic acid-7-propionic acid (X) which therefore carries the carboxyl group in the 6-position, and proved identical with the "natural" rhodoporphyrin, whose ready conversion into pyrroporphyrin was analytically demonstrated. At the same time the synthesis of 1,3,5,8-tetramethyl-2,4-diethylporphin-7-propionic acid (IX) was achieved. This proved to be identical with the "natural" pyrroporphyrin. Thus the free 6-position was also demonstrated for phylloporphyrin, for phylloporphyrin can be converted with alcoholate into pyrroporphyrin.



Pyrroporphyrin (IX) is closely related on synthetic grounds to the important blood-pigment porphyrin, mesoporphyrin (XI).

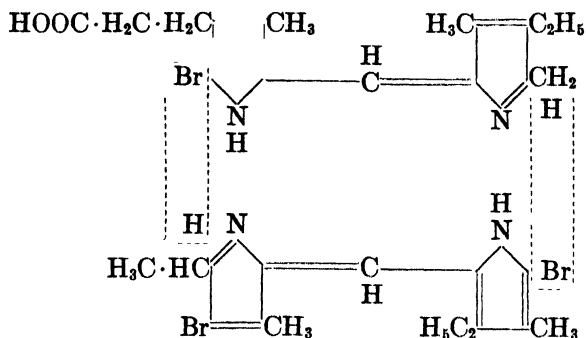
If the propionic acid residue at the 6-position in mesoporphyrin be replaced by a hydrogen atom, the formula of pyrroporphyrin results; hence we could convert pyrroporphyrin or pyrrohemine by treatment with chloromethyl ether and hydrogen bromide into bromomethyl-pyrrohemine or -porphyrin, respectively. This gave mesoporphyrin by conversion with sodium malonic ester (36). *Thus for the first time—although indeed indirectly—a common porphyrin was obtained from blood and leaf pigment; for indeed the etioporphyrins of chlorophyll have nothing to do with the etioporphyrins of blood pigment.* The "etioporphyrin of chlorophyll" proved to be a mixture of pyrro- and phyllo-etioporphyrin, corresponding in constitution to IX or XII. If both propionic acid residues are decarboxylated to ethyl groups, the formulas of the two etioporphyrins result. The proof was obtained by synthesis (6, 18, 47). Strictly speaking, moreover, the etioporphyrin of blood pigment should be considered to be, not the carboxyl-free mesoporphyrin, but the carboxyl-free protoporphyrin, whose synthesis was recently achieved (25). Recently, also, the breakdown of mesoporphyrin or mesorhodin by way of rhodoporphyrin- $\gamma$ -carboxylic acid to pyrroporphyrin has been accomplished, whereby among other products the "natural" pyrroporphyrin (IX) was obtained (9).

Phylloporphyrin proved to be a homologue of pyrroporphyrin. Spectroscopically it is markedly different from the latter, like proto- and mesoporphyrin. It is particularly sensitive to the action of hydrogen iodide, and it was necessary to consider a vinyl group linking the pyrrole nuclei in the  $\alpha$ -position, or the methyl substitution of a methine group (see XII).



XII

Ninety-six isomers were possible, but through the synthesis of pyrro-  
porphyrin the number was limited to four. All four phylloporphyrins  
were synthesized (18, 48). The scheme of the synthesis of the "natural"  
phylloporphyrin may be given here:



The complications in these syntheses were theoretically and practically  
very great. Each of the pyrromethenes employed can react with itself,  
partial decarboxylation then taking place, so that in every synthesis ten  
different porphyrins were possible, which in large part were actually formed  
and for the most part also isolated from the syntheses of all four phyllo-  
porphyrins.

$\gamma$ -Methylpyrroprophyrin (1,3,5,8-tetramethyl-2,4-diethyl- $\gamma$ -methyl-  
porphin-7-propionic acid) proved to be identical with the "natural"  
phylloporphyrin; the mixed melting point of the esters gave no depression,  
while with the three isomeric esters marked depressions were found.

Phylloporphyrin was thereby synthesized, though the constitution was  
not unequivocally established. It was still possible that a vinyl group  
could bind the pyrrole nuclei 3 and 4. Final proof of constitution was  
achieved through clarification of structure and synthesis of phylloerythrin,  
which on breakdown passes over into phyllo-, rhodo-, and pyrro-porphyrins.

For the separation of these porphyrins, as indeed for porphyrins in  
general, the fractionation method developed by Willstätter and Mieg (70)  
proved itself of great value. The basicity of the porphyrins, because of  
the imino groups contained in them, is extraordinarily varied, and by  
treatment with hydrochloric acid of graded concentrations, especially by  
several repetitions of the process, a far-reaching separation even of quite  
complicated porphyrin mixtures can be achieved. This method also  
proved itself of outstanding value in the separation of the pheophorbides.

Tswett's adsorption analysis is also fruitful in porphyrin chemistry.  
With its aid A. Treibs (65, 66, 68, 67) isolated the vanadium salts of chloro-  
phyll porphyrins and blood-pigment porphyrins from bitumen and petro-

leum, among others desoxophyllerythroetioporphyrin, whose separation from the accompanying etioporphyrins after its synthesis (23) was obtained only by the aid of adsorption analysis.

Willstätter and his pupils described numerous isomers of rhodoporphyrin, which have been subjected to a more intensive study by Treibs and Wiedemann. The result of this investigation was the discovery of a new porphyrin, verdoporphyrin, which passes over with extraordinary ease into rhodoporphyrin. The presence of verdoporphyrin probably explains the numerous porphyrins described by Willstätter and his pupils, such as erythro-, cyano-, rubi-, and glauco-porphyrin. Later pseudoverdoporphyrin was also isolated by us; this is identical with the "isorhodoporphyrin" of Conant, which the latter had obtained from purpurin (1). Isorhodoporphyrin and pseudoverdoporphyrin (26; see also 24) contain the vinyl group, as was shown through the action of diazoacetic ester and likewise through the reaction with phenyl azide. A vinyl group could thus be unambiguously demonstrated. One of the outstanding properties of pseudoverdoporphyrin is its capacity for taking up rhodoporphyrin. The separation of the two is then difficult, and the spectroscopic behavior of such a mixture is identical with the spectrum of verdoporphyrin (24).

A hydrogen bromide-glacial acetic acid mixture will add to pseudoverdoporphyrin, and through reaction with methyl alcohol a methyl alcohol addition product is obtained, which on heating—exactly like tetramethyl-hematoporphyrin—again splits off methyl alcohol with regeneration of pseudoverdoporphyrin (27).

Many of these findings were first brought up after the demonstration of a vinyl group in chlorophyll, and thence today the complicated results of the alcoholate degradation, as employed by other authors and by us, have become completely understandable. All the complications which have been exactly studied in hemin are here also at least theoretically possible, and must indeed have actually entered into individual researches. In hemin, which as is well known contains two vinyl groups, saturation of both vinyl groups to form ethyl residues occurs under the action of alcoholate; mesoporphyrin is formed. Besides, one of the two vinyl groups may be split off and one reduced, so that both isomeric hemoporphyrins arise. Besides, chlorin formation occurs from the porphyrin mixture which has arisen. Deuteroporphyrin must certainly be present also. Similar complications are naturally to be expected for chlorophyll breakdown, especially since here in the action of alcoholate widely different techniques in the manner of heating have often been employed. It is also not a matter of indifference whether one starts from phorbides or chlorophyllides. We have not as yet been able to obtain evidence for the formation of further vinylporphyrins except pseudoverdoporphyrin—

which is conveniently designated as vinylrhodoporphyrin—by alkaline degradation (by other methods all have been isolated). The individual fractions were negative to diazoacetic ester. Such vinylporphyrins might most readily be expected in the *b* series, in which, because of the neighboring position of the vinyl group and the formyl residue in the 2- and 3-positions, particular opportunity is afforded for an abnormal course of the reaction.

Parallel to this analytic-synthetic research went the study of the biological breakdown of chlorophyll, because the clarification of the constitution of substances biologically related to hemin had supplied essential starting points for the determination of the constitution and also the way to the synthesis of this substance.

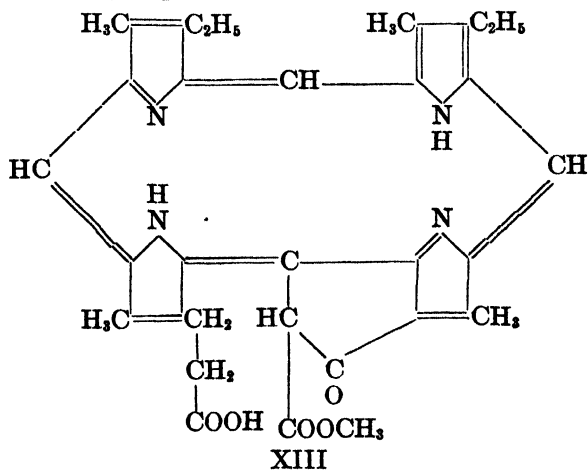
Through the investigations of Löbisch and Fischler (57) and of Marchlewski (58) phylloerythrin was known, which has been obtained from the bile of cattle or the feces of animals. From sheep feces we could obtain probophorbides *a*, *c*, and *d* (19, 21), isomeric with phylloerythrin, as well as pheophorbide *a*, pyropheophorbide *a*, dihydropyropheophorbide *a*, and pyropheophorbide *b*, which with the exception of pheophorbide *a* and the last-named *b* derivative pass over readily into phylloerythrin and are important because, as indeed their name indicates, they are spectroscopically closely related to pheophorbide and thus to the phorbides generally. Hence we must conclude that the pheophorbides as well as phylloerythrin stand in the closest relation to chlorophyll itself. In agreement with this their formation occurs in the Omasus and Abomasus (third and fourth stomachs of ruminants) as Rothmund and Inman (59) showed. Now phylloerythrin is a porphyrin (22), on the grounds of its spectroscopic behavior. Thus for the first time a basis was obtained for the view that the chlorophyll molecule also stood in close relation to the porphyrins; a possibility further supported by synthetic studies through conversion of blood pigment porphyrins into chlorins and rhodins (55, 17, 12). By bacteriological methods (19, 20) chlorophyll derivatives were likewise converted into porphyrins, again a confirmation of the relations stated above. From the conversion of chlorophyll and its derivatives into phyllo-, pyrro-, and rhodo-porphyrins the presence of the porphin nucleus could not be inferred, because in view of the brutal methods of treatment involved (alcoholate breakdown at high temperature in a sealed tube) secondary synthesis might be involved; all the more since these porphyrins are poorer in carbon than the starting material. Willstätter likewise in his book on chlorophyll (72a) had expressed himself as follows: "Also between chlorophyll and aetiophyllin and even between chlorophyll and the first dibasic porphyrins such as cyanoporphyrin or erythroporphyrin lie two steps which essentially transform the molecule, and which cannot be brought into parallel with the reactions of hemin."

"One step is the delactamization and relactamization of the chlorophyll components, through which one ring system is broken and a new one synthesized. The second rearrangement of the molecule, which takes place less obviously, occurs through the action of alkali at high temperatures and leads from the chlorophyllins to the more simply constituted dibasic phyllins, or from phytochlorin and phytorhodin to the corresponding porphyrins."

And somewhat further on: "Therefore it is more probable that the lactam group is of the pyridone type, its carboxyl therefore itself a ring constituent, and that the fourth pyrrole nucleus of cyanoporphyrin first arises through removal of a carbon atom."

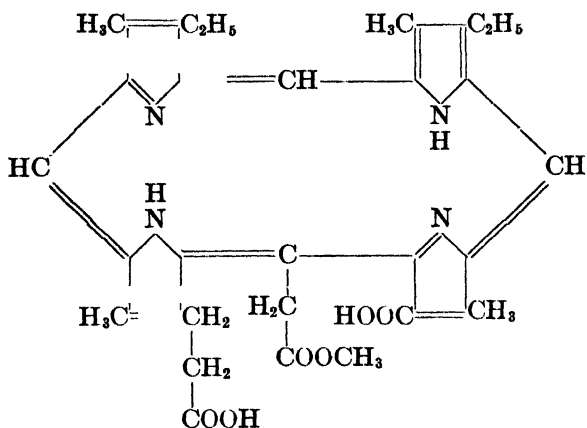
It was necessary to search for methods which, while preserving the carbon framework of chlorophyll, should lead to porphyrins, for which synthetic methods stood available. Cautious reduction with hydriodic acid and glacial acetic acid proved fruitful in results here; application of this method to pheophorbide and to chlorin *e* yielded fundamentally different results. The pheophorbides gave pheoporphyrins; chlorin *e* gave chloroporphyrins (3, 4, 31, 32, 33, 34, 10). Spectroscopically, essential differences between the two classes were manifest. In the pheoporphyrins the second and third absorption bands appear compressed, as in the spectroscopic picture of phylloerythrin, while in the chloroporphyrins the spectral phenomena are much more similar to those of the blood pigment porphyrins.

Numerous porphyrins were isolated, and their constitution determined, which cannot be discussed in more detail in a short lecture. The most important among them is pheoporphyrin *a*<sub>8</sub> (11, 15) (XIII) which is obtainable from the pheophorbides, also from pheophytin and chlorophyll-



lide, and which always occurs as a monomethyl ester (51, 33, 34); indeed the carbomethoxyl residue in position 10 is only saponifiable with diffi-

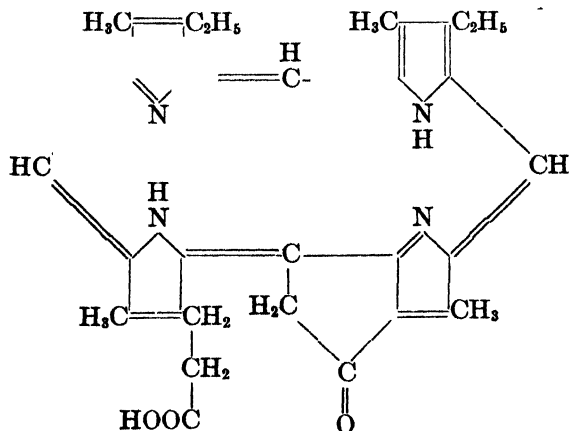
culty. Pheoporphyrin  $a_5$  reacts with ketone reagents and can be split by hydrolysis to chloroporphyrin  $e_6$ , which is likewise a monomethyl ester and possesses the following formula (XIV):



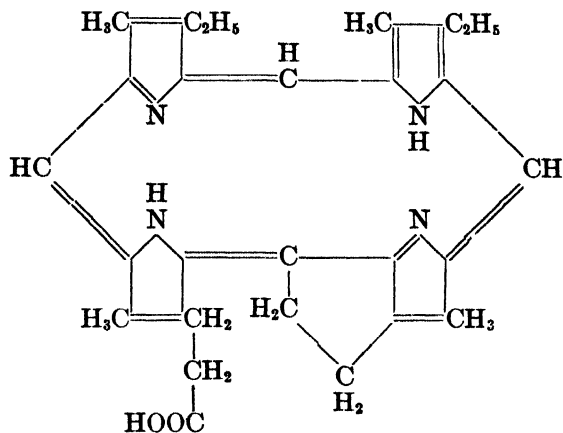
XIV

For, on the one hand, it can readily be reconverted into pheoporphyrin  $a_5$ ; on the other hand, it passes over on treatment with 30 per cent methyl alcoholic potassium hydroxide into chloroporphyrin  $e_4$  (through replacement of the  $\text{COOCH}_3$  residue by H (XVIII) and rhodoporphyrin (through replacement of the  $\text{CH}_2\text{COOCH}_3$  residue by H) (X). Through the transformation of chloroporphyrin  $e_6$  into pheoporphyrin  $a_5$ , and its reversal, a transition between the chloroporphyrins and the pheoporphyrins was brought about for the first time, and the presence of a carbomethoxylated isocyclic ring in chlorophyll was made probable.

Pheoporphyrin  $a_5$  (XIII) on decarboxylation passes over readily into phylloerythrin (XV):

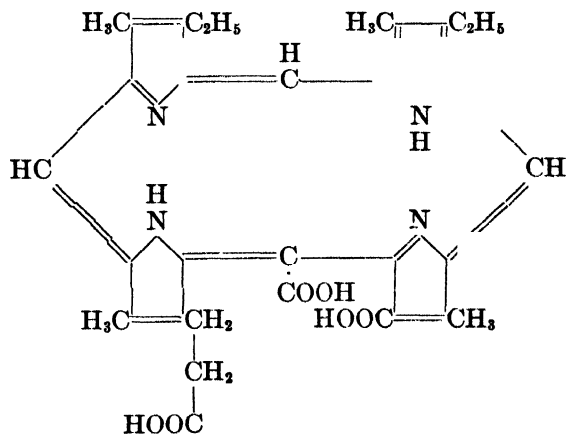


Phylloerythrin may be readily reduced to desoxophylloerythrin (XVI), which contains only two atoms of oxygen, and these are in a carboxyl



XVI

group. The constitution of phylloerythrin was demonstrated as follows: Phylloerythrin does not react with alkalis in an atmosphere of nitrogen, but in the presence of oxygen breakdown occurs to the characteristic chlorophyll porphyrins, phyllo-, pyrro-, rhodo-porphyrin, and rhodo-porphyrin- $\gamma$ -carboxylic acid (XVII) which was first obtained by this method; this behavior can only be explained by an ethanone bridge between C<sub>6</sub>



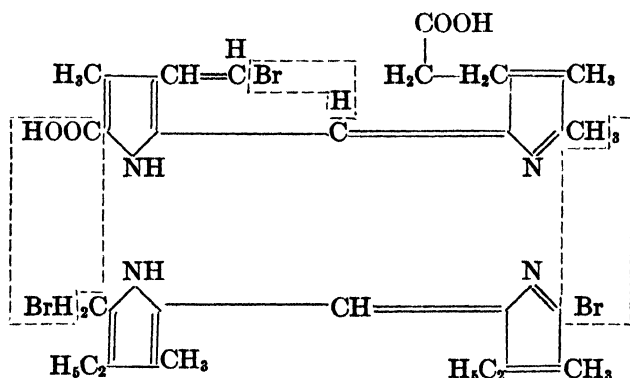
XVII

and the  $\gamma$ -methine group. The keto group could be certainly demonstrated through reaction with ketone reagents.



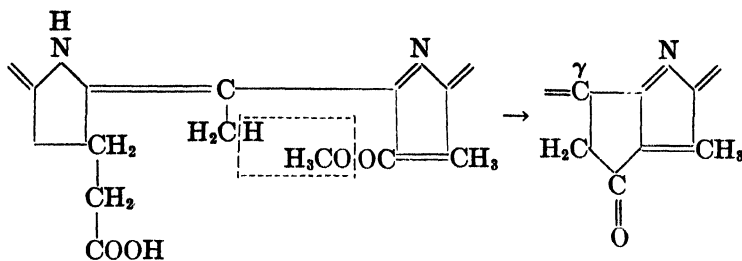
The constitution of desoxophylloerythrin and of phylloerythrin, however, could also be demonstrated by synthesis (37, 39, 40, 16). On the basis of elementary analysis only the formula of a monocarboxylic acid (page 43) or the ring formula (XVI) with two less hydrogen atoms, stood available for desoxophylloerythrin. Fortunately all eight monocarboxylic acids (page 43) had already been synthesized. Spectroscopic observations had already excluded identity (the spectroscopic difference due to the linked isocyclic ring is not in itself large). A new spectral type arises as the  $C=O$  group adjoining nucleus III enters (compare formula XV). The spectroscopic influence will be of interest in the iso compound, with  $CO$  adjoining the  $\gamma$ -position. The synthesis of an isophylloerythrin is under way; likewise the mixed melting points gave marked depressions. Only the ring formula, therefore, remained possible.

The synthesis was carried out according to the following scheme, and gave a substance which proved to be identical with the "natural product" in all its properties (38). Desoxophyllerythrin gave, on oxidation with



fuming sulfuric acid containing sulfur, phylloerythrin along with chlorophyllin  $e_8$ . We admit that the position of the  $CO$  group at 9 in phylloerythrin is not proved by this synthesis. It might equally well be in the 10-position; but the result of the degradation of phylloerythrin which leads, as stated, to the porphyrins pyro-, phyllo-, and rhodo-porphyrin, demonstrates unequivocally the position of the carbonyl group.

Recently (35) we have demonstrated in another manner by direct synthesis the constitution of phylloerythrin, employing the action of sodium ethylate on chlorophyllin  $e_4$ , according to the following formulation.



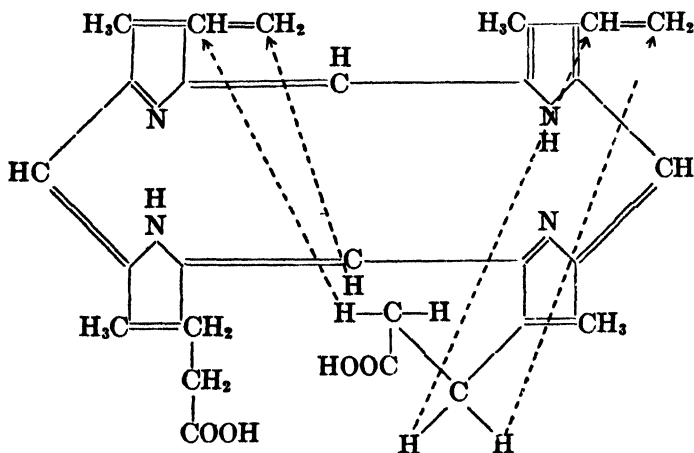
XVIII

XV

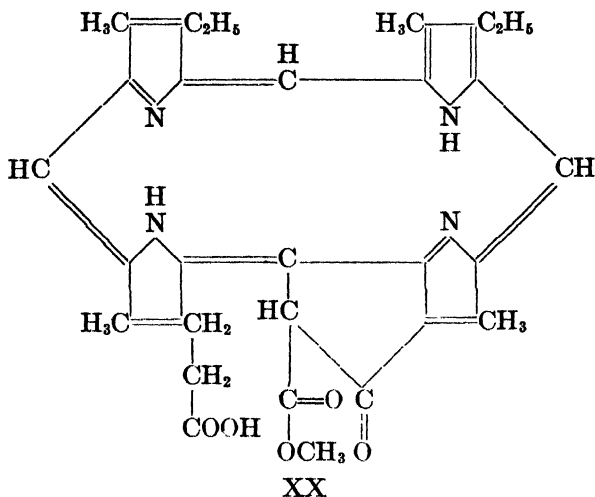
Through the proof of the constitution of phylloerythrin, that of phylloporphyrin as a methyl-substituted pyrroporphyrin was also determined, and the  $\gamma$ -position once more proved.

Let us now summarize briefly the most important results of this section:

Chlorophyll is a pyrrole pigment, esterified with phytol and methyl alcohol. It contains magnesium, bound in complex linkage. Fundamental to it is the porphin system, built into which is an isocyclic ring with a keto group at 9 and a carboxymethyl group at 10; otherwise in respect to the arrangement of the substituents it corresponds to etioporphyrin III and therefore to the hemin of hemoglobin. One may also picture the most important of the chlorophyll porphyrins, pheoporphyrin  $a_b$ , as derived from protoporphyrin through  $\beta$ -oxidation of the propionic acid residue in the 6-position to a ketopropionic acid, and condensation, with loss of water, between carbon atom 10 and the  $\gamma$ -methine group of the porphin nucleus, with saturation of both vinyl groups of protoporphyrin to give ethyl residues, as illustrated by the following formulas:



XIX



From a purely formal point of view, one may thus regard pheoporphyrin  $a_6$  as a monoxide of protoporphyrin, and pheoporphyrin  $b_6$  as an oxidation product of pheoporphyrin  $a_6$ , in which the methyl group in the 3-position is replaced by the formyl group.

For the porphyrins in general A. Stern and H. Wenderlein (62) have determined the pyrrolenine structure of two opposite nuclei on the basis of the varying influence on light absorption by the carbonyls in the porphin system, according to the position on the nucleus.

Further, the attachment of the phytol group to the propionic acid residue has been demonstrated, and that of the methoxyl to the carboxyl group of the isocyclic ring.

Through degradation of pheophorbide with diphenyl at 180–250°C., Conant has obtained free pyropheophorbide. This method of investigation is open to possible objection because of the high temperature and possible re-esterification of the pheophytin through the alcohol employed. The decarboxylation, however, can be carried through with the same result using boiling pyridine, and pheoporphyrin  $a_7$  (rhodoporphyrin- $\gamma$ -glyoxalic acid methyl ester) has always been observed only as a monomethyl ester, esterified on the  $\gamma$ -glyoxyl side chain, giving on degradation free rhodoporphyrin (52). Ethyl chlorophyllide also gave the ethyl ester of phylloerythrin (52). Finally pheophytin, obtained with acetone, after preparation and separation of the pheophorbide components  $a$  and  $b$ , gave on decarboxylation the free pyro compounds (8).

#### CONCERNING PHEOPHORBIDE, PYROPHEOPHORBIDE, AND CHLORIN $e$

Pheophorbide, just like chlorophyllide and chlorophyll, is transformed to pheoporphyrin  $a_6$  (XIII) and chlorin  $e$  into chloroporphyrin  $c_6$  (XIV) by

means of glacial acetic acid-hydrogen iodide mixture. The constitution of the former is confirmed as above and their reciprocal interconversion is possible. Thus it appears that in pheophorbide the same isocyclic ring must exist as in pheoporphyrin  $a_6$ , while in the side chain chlorin  $e$  must correspond to chloroporphyrin  $e_6$ . This is confirmed also by the fact that pheophorbide is transformed practically quantitatively by means of diazomethane-methyl alcohol into chlorin  $e$  trimethyl ester; the same transformation also occurs with the aid of phosgene-alcohol. Pheophorbide, as well as pheoporphyrin  $a_6$ , yields a well-crystallized oxime which is convertible by means of hydriodic acid into pheoporphyrin  $a_6$  oxime (43; cf. 28, 49). Accordingly chlorin  $e$  should be convertible back to pheophorbide. Actually this reaction occurs, but with a yield of only 10 per cent. Decarbomethoxylation occurs so that not pheophorbide but pyropheophorbide results. The latter may also be obtained by boiling pheophorbide with pyridine. Biologically this process occurs in the digestive tract of the ruminants.

The splitting of the carbomethoxyl residue and the low yield of the re-synthesis is quite surprising. In remarkable fashion, however, the yield may rise to about 100 per cent if chlorin  $e$  is esterified in the 6-position with glycol.

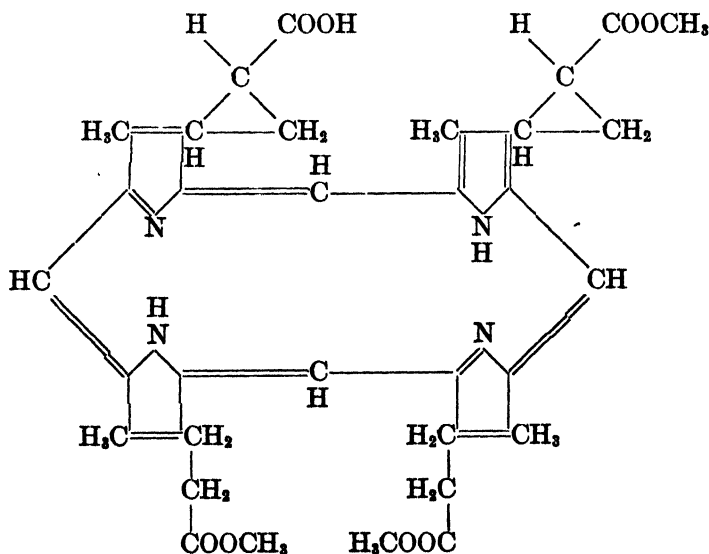
Reduction of pheophorbide as well as unchanged chlorophyllide and chlorophyll by means of hydrogen iodide yields only pure pheoporphyrin  $a_6$  (53). In the digestive tract, where strong reduction processes may often be found, there occurs among other porphyrins phylloerythrin, and thus the porphyrins were early considered to be reduction products of chlorophyll. Synthetically porphyrins were converted into chlorins by reduction methods, and accordingly the porphyrins should be regarded as oxidation products of the phorbides and chlorins. Finally it was possible by means of synthetic methods, this time by oxidation of the porphyrins, to produce substances similar to the chlorins, whereby the latter appeared to be oxidation products of the porphyrins. Clarification of the difficulty was obtained only slowly. Elementary analyses first showed the extraordinary similarity in composition between pheoporphyrin  $a_6$  dimethyl ester and methylpheophorbide as well as between chlorin  $e$  trimethyl ester and chloroporphyrin  $e_6$  trimethyl ester, so that the possibility of isomerization was brought to the fore.

The calorimetric investigations of A. Stern and G. Klebs were then of great importance. These authors showed that the energy contents of methylpheophorbide and pheoporphyrin  $a_6$  dimethyl ester were equal. Likewise the energy contents of chlorin  $e_6$  and chloroporphyrin  $e_6$  trimethyl ester were equal. The formula, therefore, of pheoporphyrin  $a_6$  must be essentially the same as that of pheophorbide, and the formula of chloroporphyrin  $e_6$  essentially the same as chlorin  $e$ . We thus enter into the dis-

cussion of the phorbide or chlorin state of chlorophyll, in which extraordinary difficulties appeared, since in the side chains chlorophyll and its derivatives were generally regarded as saturated. Consequently isomerism among the porphyrins, the phorbides and the chlorins could not be a correct explanation and contradictions appeared on every side. The possibility of methylene groups as bridges between the pyrrole nuclei or of pyrroline formation (17, 12) was brought into discussion. The latter explanation, which was primarily applied to the synthetic chlorins, was difficult to apply to the "natural" products, since according to the state of knowledge at that time, a higher hydrogen content must occur in the latter molecules than in the porphyrins. Actually, however, isomerism did exist.

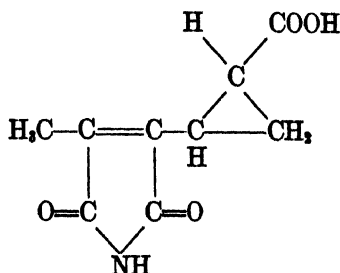
THE DISCOVERY OF A VINYL RESIDUE IN THE PHORBIDES, CHLORINS,  
PURPURINS, AND PORPHYRINS OF CHLOROPHYLL

If one allows colorless hydrogen iodide to act upon phorbides or chlorins, acetylporphyrins are obtained (42). The acetyl group occupies the 2-position, a fact which was verified synthetically (44). A still more positive indication of the presence of the vinyl group is shown by the reaction with diazoacetic ester (30). Protoporphyrin contains two vinyl groups and reacts with two molecules of diazoacetic ester to yield 1,3,5,8-tetramethyl-2,4-dicyclopropylcarboxylic acid ester-porphin-6,7-dipropionic acid.



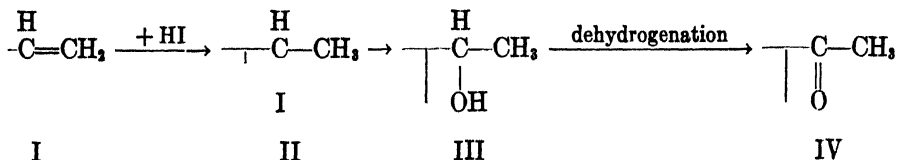
XXI

The constitution of this substance was proved, not only by the elementary analysis, but by oxidation. Besides hematinic acid, methylmaleic imide-cyclopropyl-carboxylic acid was obtained, with the following formula:



XXII

In the same fashion, the phorbides, chlorins, and purpurins reacted with diazoacetic ester. For example, pheophorbide after the reaction and subsequent oxidation yields methylmaleic imide-cyclopropyl-carboxylic acid as well as methylethylmaleic imide and hematinic acid. Therefore the vinyl group must exist in pheophorbide and at the same time it is shown that the diazoacetic ester reaction is generally applicable to the detection of vinyl radicals in the porphyrins as well. Thus the vinyl group may be detected in pseudoverdoporphyrin, in phyllochlorin, and in rhodochlorin. The appearance of the acetyl radical in the oxoporphyrins may be explained by the presence of the vinyl group, according to the following scheme:



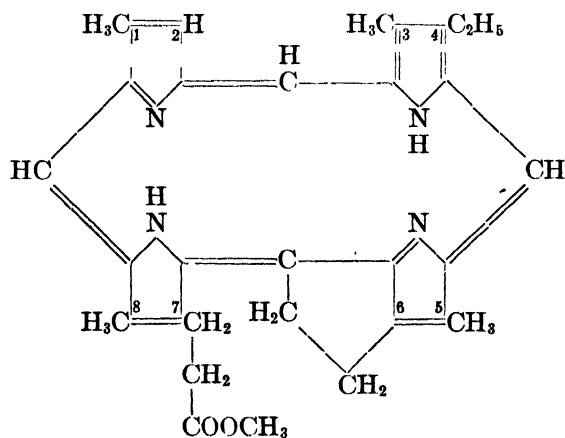
At first hydrogen iodide adds to the vinyl group, then the iodine is exchanged for hydroxyl, and finally spontaneous dehydrogenation leads to the acetyl radical. The reaction is completely analogous to the hemato-porphyrin reaction of hemin, except that state III represents the end point of the latter.

Hydrogen bromide as well as methyl alcohol (26) combine with the vinyl groups of chlorophyll derivatives as they do with those of hemin. By means of catalytic reduction or glacial acetic acid-hydrogen iodide reduction, hemin is converted into mesohemin, containing four more hydrogen

atoms. This reaction similarly converts bilirubin to mesobilirubin. Exactly in this fashion the meso derivatives of chlorophyll may be obtained,<sup>2</sup> and one may prepare mesopheophorbide, mesochlorin, etc., in this way. The mesoderivatives are spectroscopically still phorbides or chlorins, but contain two hydrogen atoms more than the corresponding porphyrins. Consequently, during the conversion into the porphyrin a dehydrogenation must take place.

*Proof of the 2-position of the vinyl group*

It was of especial interest to determine the position of the vinyl group in the molecule. This was accomplished after treatment of oxophylloerythrin with concentrated hydrochloric acid in the pressure bomb (14). Two porphyrins resulted, a phylloerythrin with a free methine group and, by means of a secondary degradation, a pyrroporphyrin which contained a second free methine group. The latter was synthesized (7). No depression of the mixed melting point was observed. A further proof was started by the degradation of oxophylloerythrin with hydrogen bromide-glacial acetic acid. There resulted a reduction of the keto group of the isocyclic ring, together with the splitting off of the acetyl group. The product was a desoxophylloerythrin with a free methine group. Inasmuch as at that time it was not decided whether a formyl or an acetyl group was present in the oxoporphyrins, the four theoretically possible desoxophylloerythrins with a free methine group in either position 1, 2, 3, or 4 were synthesized (44). The desoxophylloerythrin ester of the following formula



XXIII

<sup>2</sup> The addition of two hydrogen atoms was first correctly indicated by Stoll and Wiedemann (Helv. Chim. Acta **16**, 191 (1932)), but no experimental details were given. The authors assumed addition to a double bond in the nucleus.

gave no depression in mixed melting point with the analytical preparation, whereas the other three showed differences even spectroscopically.

With this determination, definite proof of the presence of an acetyl residue in the oxoporphyrins was obtained and thereby that of the vinyl group in the original material. Likewise the position of the substituents in "natural" hemin was confirmed.

A third proof was yielded by the displacement of the ethyl residue in oxorhodoporphyrin by means of bromine. The bromine was removed by catalytic reduction and there resulted a rhodoporphyrin with a free methine group. That it was a 2-desethylrhodoporphyrin was proved by means of a mixed melting point with the synthetic material (7). The acetyl group was re-introduced into the 2-desethylrhodoporphyrin and oxorhodoporphyrin re-obtained. Thus through synthesis the constitution of oxorhodoporphyrin and the oxo compounds was confirmed (26).

In this manner the detection of the acetyl group in the oxoporphyrins was confirmed at the same time. Earlier we had assumed a formyl residue; however, of course, only an ethyl group can be located in the 2-position.

For the determination of the constitution of chlorophyll and its derivatives, the demonstration of a vinyl group was fundamental, for then for the first time the easy isomerization of the green substances to the red substances was understandable. There was required merely a rearrangement of hydrogen to the vinyl group in order to obtain the saturated porphyrin system, for the porphyrins obtained from chlorophyll did not contain the vinyl group at all. Also the biological origin of phylloerythrin becomes understandable. In addition, the higher energy content, corresponding to two hydrogen atoms, of the meso compounds and of the diazoacetic ester addition products becomes clear (60).

An excess of two hydrogen atoms over the saturated porphyrins was thus known to be present in the green meso compounds, while the pheophorbides were isomeric with the corresponding porphyrins but, exactly like the meso compounds, it was necessary that they contain two hydrogen atoms more in the nuclear system (those atoms removed from the ethyl residue). The question then arose as to the position of these hydrogen atoms. This was answered through the detection of the optical activity of rhodochlorin, of phyllochlorin, of pyrochlorin, and of their meso compounds.

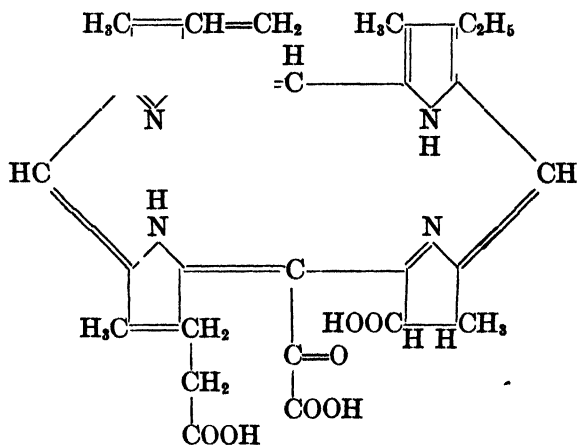
#### ANALYSIS OF THE OPTICAL ACTIVITY OF CHLOROPHYLL

Pheoporphyrin  $a_6$  and pheophorbide possess a center of asymmetry in carbon atom 10 and therefore chlorophyll can be optically active (54). The optical activity was first pointed out by Stoll and Wiedemann (64), who observed a small rotation—close to or within the limits of error—which quickly vanished. We could confirm the optical activity of chloro-



phyll and numerous derivatives, but not the rapid inactivation. Even many hours of boiling with pyridine led to no inactivation. Transformation into the leuco compound followed by re-oxidation did not always lead to loss of optical activity. Chlorophyll and its derivatives are levorotatory, with the exception of those substances which are prepared by the aid of propyl alcohol and potassium hydroxide, a reagent which was introduced into chlorophyll chemistry by Conant and leads to the purpurins. These are all dextrorotatory. If one, however, conducts the purpurin reaction with the aid of sodium hydroxide in the presence of air, then levorotatory pseudochlorin  $p_6$  is the result.

This is the place to consider briefly the purpurins which, as mentioned, were discovered by Conant.<sup>3</sup> Propyl alcoholic potassium hydroxide acts readily in the cold on chlorophyll, pheophorbide, and chlorins with cleavage of the isocyclic ring. There result unstable chlorins which are transformed into purpurins by the action of diazomethane. Conant found two purpurins, namely, purpurin 7 and purpurin 18. The latter contains one carbon atom less than purpurin 7. Purpurin 7 has the following formula:

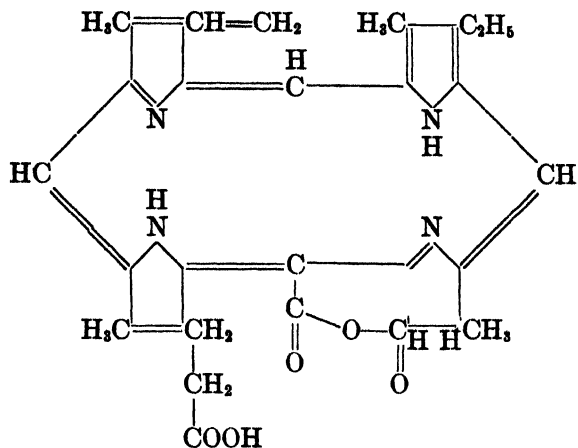


XXIV

That the vinyl group is present was proved by the reaction with diazoacetic ester, the oxo reaction, and by means of the degradation to rhodochlorin, whereby the glyoxalic acid residue is split off. That rhodochlorin contains the vinyl group follows from its transformation into vinylrhodophyrin.

<sup>3</sup> According to L. Marchlewski (Biochem. Z. **277**, 17 (1935)) and Conant, purpurin 18 was first observed by the former and described as anhydro- $\beta$ -phyllotaonin.

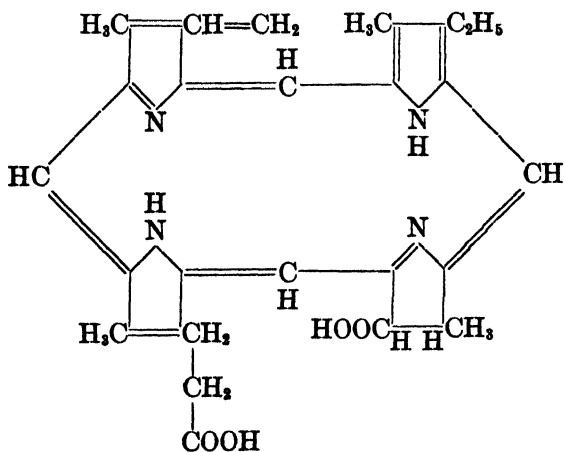
Purpurin 18 has the following formula :



XXV

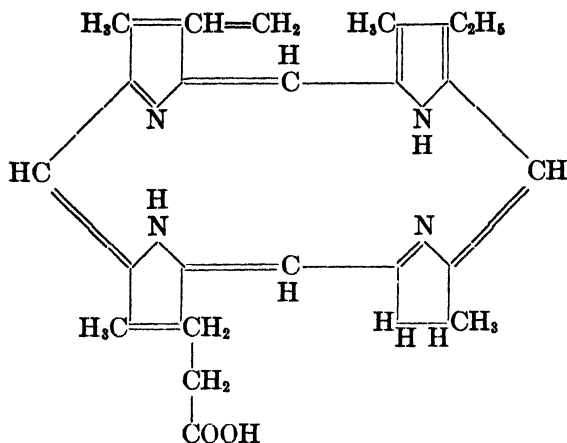
The vinyl group of this compound is identified in the same fashion as was that of purpurin 7.

As the purpurin structures indicate, an extensive oxidation of the isocyclic ring is involved here, very similar to that which can occur by treatment of chlorin *e* with hydrogen iodide in the presence of excess iodine. We cannot enter further into the details of this process here. The purpurins are also optically active. They may be transformed into optically active chlorins, among which the following may be mentioned :

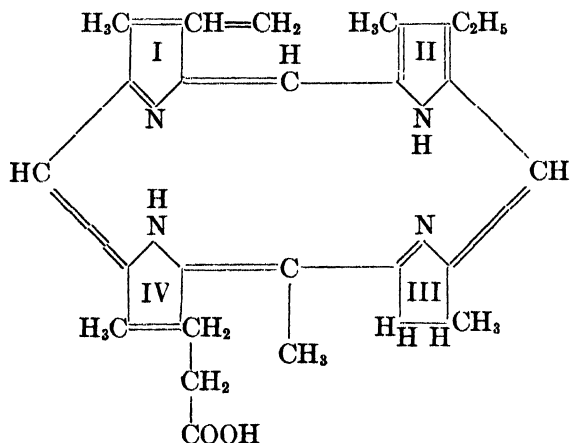


XXVI

Rhodochlorin



XXVII  
Pyrrochlorin



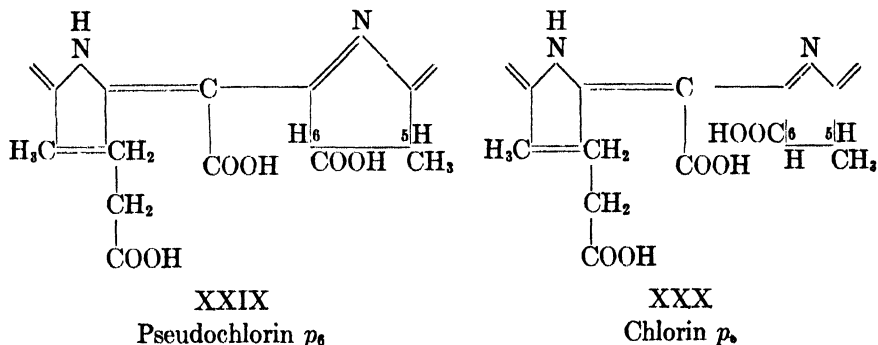
XXVIII  
Phyllochlorin

These three substances are also optically active and may isomerize into the corresponding optically inactive porphyrins. For chlorophyll, the chlorins, and the purpurins, accordingly, formulas with methylene groups cannot be considered, since with these optical activity could not be present. There remains only the assumption of a pyrrolenine structure for one ring, and most probably ring III comes into question. In the isocyclic ring double bonds could not occur, inasmuch as in such a system powerful strains would be set up. For this reason the other rings of the system are

generally laid down in terms of the formulas previously employed. That rings I and II are to be formulated differently followed from the spectroscopic findings of the four synthetic  $\beta$ -free desoxophylloerythrins (45). A pyrrolenine structure for rings I and III in the porphyrin nucleus was then found by A. Stern and H. Wenderlein (61), and because of this it is highly probable that chlorophyll itself must have an analogous arrangement, for the spectroscopic appearance of chlorophyll derivatives is fundamentally very similar to that of porphyrins. That ring III possesses the pyrrolenine structure is proved in the following way: As already mentioned, chlorin  $p_6$ , which is dextrorotatory, may be obtained from

a. Degradation by sodium hydroxide and air produces  $p_6$  and  $p_6$ . The latter is distinguished from chlorin  $p_6$  by means of the following properties: spectroscopically, and by the opposite sign of rotatory dispersion. The two substances are, however, not optical antipodes.

In similar fashion, mesopheophorbide may be transformed into the analogous meso derivatives; likewise the diazoacetic ester addition products. Both series, however, are isomeric with each other, as the elementary analyses show. The explanation for this behavior is given by considering the isomerism in the sense of the following formulas:

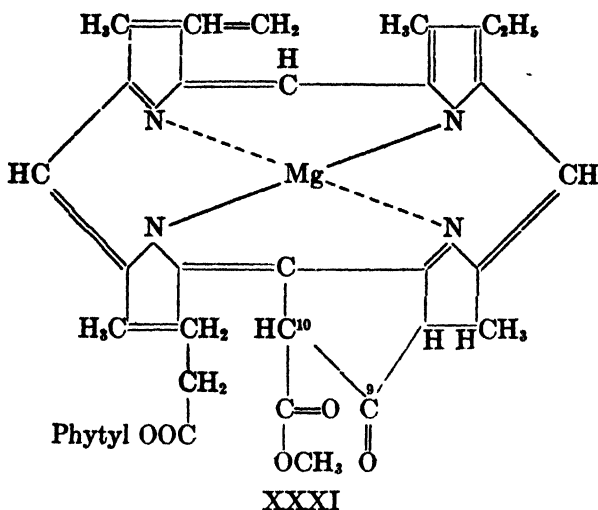


That the molecules are not optical antipodes may be seen from the models without difficulty, for the asymmetric center on carbon atom 5 does not participate in the process.

Since, as already mentioned, the analogous substances, this time with opposite rotations, were prepared from the diazoacetic ester and meso derivatives of the pheophorbides, we regard the formulation of ring III as a pyrrolenine ring as certain, inasmuch as only thus could optical antipodes be formed. That the carboxyl groups on carbon atom 6 are differently arranged in space follows also from the fact that in the chlorin  $p_6$  series the anhydride formation to purpurin 18 is possible, whereas in the pseudo

series this does not take place. A steric difference must therefore exist. The spectrographic investigation of A. Stern and H. Wenderlein of the various substances under consideration confirms the same idea (63).

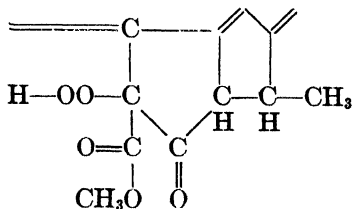
Consequently, for chlorophyll *a* itself only the following formulation comes into question:



This formula is capable of explaining all the transformations, and any other choice in the location of the double and single bonds is now excluded. This structural formula has on the tertiary carbon atom 10 a hydrogen atom which must be characterized by a special lability, since a carbonyl group and a carbomethoxyl group are located next to it. This explains two important properties of chlorophyll,—allomerization and the phase test.

By allomerization is understood the phenomenon that alcoholic solutions of chlorophyll or chlorophyllides, evaporated to dryness, lose their ability to crystallize and the phase test becomes negative, i.e., the green phase immediately appears. We owe to Conant the explanation of this process—namely, that one mole of oxygen is used up per mole of chlorophyll—and we were able to show that oxidation occurred on C<sub>10</sub>. The allomerization process could be imitated in an alcoholic medium with quinone, which forms hydroquinone, and after hydrogen iodide reduction 10-ethoxy- or 10-methoxy-pheoporphyrin *a<sub>8</sub>* could be isolated. The process takes place in the following fashion: Chlorophyll adds to quinone in the 1,6-positions to form the hydroquinone ether (Wieland), which then decomposes by alcoholysis. 10-Ethoxypheoporphyrin *a<sub>8</sub>* as well as 10-ethoxypheophorbide could be isolated. In the presence of alcohol and

air—as in the classic allomerization—the 10-peroxide derivative of the following formulation must arise:



This was, however, not isolated as such, but the hydrogen iodide reduction yielded pheoporphyrin *a*<sub>7</sub>, whereby the oxidation on carbon atom 10 may be said to be proved. It is interesting as well as important to point out that the activation of the hydrogen atom on carbon atom 10 is intensified by the coordinately bound magnesium.

In the case of pheophorbide the process could not be imitated with iodine-alcohol, in contrast to chlorophyllide *a* and pheoporphyrin *a*<sub>6</sub>, which easily undergo the transformation. In pheoporphyrin *a*<sub>6</sub> the 10-hydrogen atom is therefore more labile than in pheophorbide, while this exhibits no increased reactivity in its phyllin; it is especially insensitive toward atmospheric oxygen.

In regard to the phase test, this is introduced by the formation of the yellow potassium salt arising from the wandering of the hydrogen atom from carbon atom 10 to the carbonyl group in 9. Through this process a double bond is formed between 9 and 10. The ring becomes more labile, as the construction in the model illustrates very clearly, and the tendency to ring cleavage is great. It thus becomes plain why hydrolysis under the influence of methyl alcoholic potassium hydroxide proceeds extraordinarily easily with such enormous reaction velocity that within thirty seconds it is quantitatively complete and chlorin *e* is formed. Pure chlorin *e*, free from unstable chlorins and purpurins, is the criterion for undamaged chlorophyll. Methanolysis with the aid of diazomethane is still easier to carry out; in the presence of uninjured chlorophyll only chlorin *e* trimethyl ester is produced by this reaction (41). In agreement with this the 10-oxy derivatives of pheophorbide give no phase test, inasmuch as the hydrogen atom needed for the formation of the enol group on C<sub>9</sub> is missing. For the same reason, allomerized chlorophyll is phase test negative.

It is impossible to go farther into the question of chlorophyll *b*. It may be mentioned that this is constituted in complete analogy to chlorophyll *a*, except that in place of the methyl group in ring II a formyl residue is present.

Purely formally, hemin and chlorophyll are closely related in respect to the fundamental ring system of each, as follows from the explanation on page 53. The most important differences are the complexly bound metal, in the former case iron, in the latter magnesium, in the former free carboxyl groups, in the latter a double esterification,—once with phytol and once with methyl alcohol.

In historical development we regard hemin as the older dyestuff. How it became transformed into chlorophyll is not clear. Perhaps there resulted at first a methylation on the  $\gamma$ -carbon atom; from our synthetic studies we found that derivatives of phylloporphyrins with unsaturated side chains in the 6-position close to form isocyclic rings even under the mildest conditions.

Further progress in knowledge in this field is to be expected on the synthetic side and also on the analytic through studying the chlorophyll of lower plants. Since the sulfur bacteria possess a modified chlorophyll in which in place of the vinyl group an acetyl radical is present, the possibility exists that further differently constituted types of chlorophyll appear in nature.

These investigations have been performed during the past seven years in the Organic-Chemical Institute of the Technische Hochschule in Munich.

I owe many thanks to my numerous collaborators, who are named in publications appearing in Liebigs *Annalen*.

Furthermore, the work has benefited through use of the excellent apparatus of Dr. Neumann. Particularly the extraction apparatus has effected an unusual cheapening of the costs and acceleration of operation. The countless microanalyses have been performed by Dr. J. Unterzaucher and his colleagues.

I am most deeply indebted to the Rockefeller Foundation and the Deutschen Forschungsgemeinschaft (Notgemeinschaft der Deutschen Wissenschaft) for pecuniary assistance.

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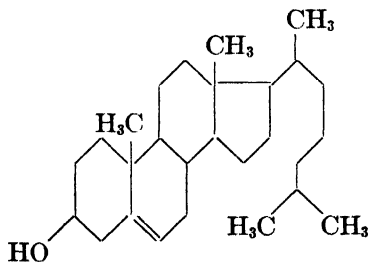
# THE MALE SEX HORMONES<sup>1</sup>

L. RUZICKA

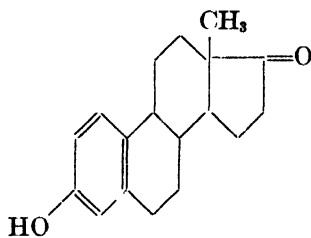
*Technische Hochschule, Zürich, Switzerland*

*Received October 29, 1936*

In the last few years investigations of the sex hormones have resulted in a remarkable increase in the knowledge of the relationship between chemical constitution and physiological activity. The astonishingly rapid development of the chemistry of the sex hormones was due to a fortunate accident: researches in this field were begun at the time that the study of the constitution of cholesterol was being brought to a close. Through the collective efforts of a number of investigators, especially Windaus, Wieland, Diels, and Rosenheim, it was possible in 1932 to propose with certainty formula I for cholesterol. In the meantime, the chemistry of the hormones of the sex gonads had reached a point which indicated the probable relationship to the sterols and thus permitted the use of the extensive knowledge in this latter field.



I  
Cholesterol



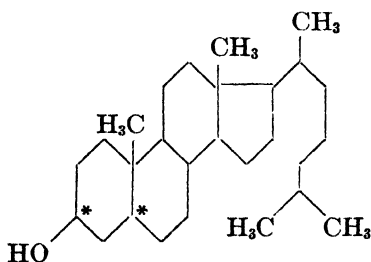
II  
Estrone

By the use of the Allen-Doisy test as a quantitative guide, Doisy in the United States and Butenandt in Germany succeeded in 1929 in isolating from pregnancy urine the first pure sex hormone, now generally known as estrone. This female hormone has the empirical formula  $C_{18}H_{22}O_2$ , and its chemical investigation in the laboratories of Butenandt, Doisy, and Marrian indicated the presence of a phenolic group, of a ketonic group,

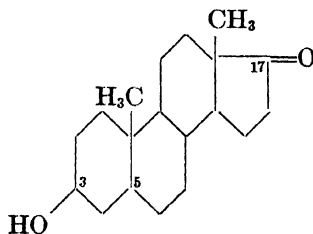
<sup>1</sup> A paper delivered at the Tercentenary Conference of Arts and Sciences at Harvard University, September, 1936.

and of four rings. Since the only tetracyclic ring system previously observed in the animal kingdom had been found in the sterols and bile acids, it was assumed by Rosenheim and Bernal that the estrone molecule might be a derivative of the same skeleton. The simplest expression for estrone, on the basis of the known facts and on the assumption of a relationship to cholesterol, is given by formula II which was proposed by Butenandt. All the subsequent chemical work, of which the investigations of Cook in 1935 and of Marker in 1936 should be mentioned especially, proved to be in perfect agreement with this formula. Only the complete steric relationship of estrone to cholesterol remains to be determined.

Androsterone, the first male hormone to be isolated, was obtained from male urine by Butenandt and Tscherning in 1931. The cock's comb test, developed as a quantitative procedure by Koch, Moore, and Gallagher in 1929, was used as an assay method. If this hormone,  $C_{19}H_{30}O_2$ , which possessed both ketonic and alcoholic groups, was to be regarded as a simple derivative of a sterol, then it might be represented as a degradation product of a hydrogenated sterol (III) from which the side chain had been removed. Based on this assumption, formula IV for androsterone was proposed by Butenandt.



III  
Cholestanol or a  
stereoisomer

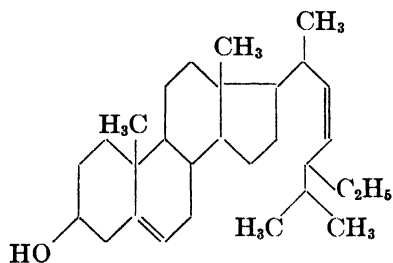


IV  
Androsterone or a  
stereoisomer

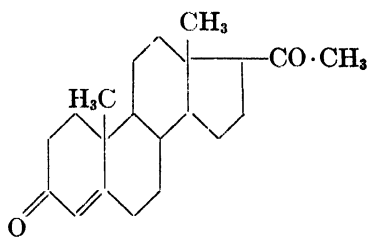
The amount of androsterone available for investigation was so extremely small that no support for this formula could be obtained by the usual degradation methods. In 1933, therefore, with the help of Goldberg, Meyer, and Brünger, investigations were undertaken in the laboratories of the Technische Hochschule in Zürich to determine the constitution of androsterone by an essentially synthetic procedure. The method which proved to be successful was the destructive oxidation with chromic acid of the acetates of the four available stereoisomeric dihydrosterols of formula III: cholestanol, epicholestanol, coprostanol, and epicoprostanol. These stereoisomers are distinguished by the configuration of carbon atoms 3 and 5 of the sterol nucleus. Fortunately, it was possible by the oxida-

tion of the saturated sterol acetates with chromic acid to obtain in small yields the acetates of the corresponding oxyketones (IV), which were then saponified. The four stereoisomeric oxyketones,  $C_{19}H_{30}O_2$ , were thus prepared, and that derived from epicholesterol proved to be identical with androsterone. In this manner the relationship between a sex hormone and the sterols was definitely established for the first time.

Very shortly thereafter both Butenandt and Fernholz, also by the use of synthetic methods, proved the constitution of the corpus luteum hormone, progesterone. Since this hormone was shown to be an unsaturated diketone,  $C_{21}H_{30}O_2$ , and on the assumption that it might be a sterol derivative, formula VI was proposed as a hypothetical expression for this substance. Subsequently, stigmasterol (V) was converted by stepwise degradation to a diketone identical with progesterone.



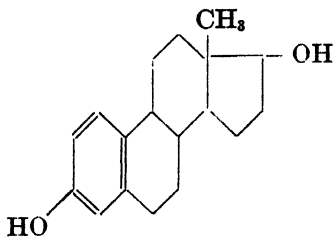
V  
Stigmasterol



## VI Progesterone

The question now arose as to whether estrone, androsterone, and progesterone were the only naturally occurring compounds possessing sex hormonal action, and also as to whether synthetic compounds with similar physiological properties might not be prepared.

Schwenk and Hildebrandt discovered that the reduction product of estrone in which the ketonic group had been converted to a secondary alcohol (VII) has an activity several times greater than that of estrone itself. This substance, estradiol, was later isolated by Doisy from ovaries and proved to be the most active hormone of the estrane series.



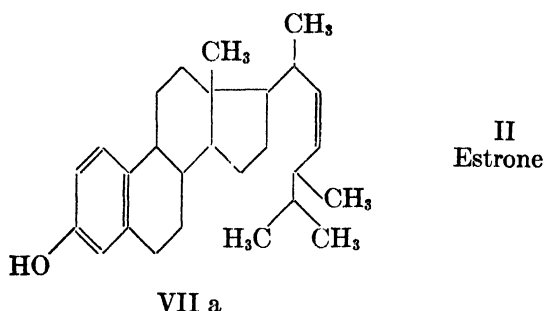
## VII

### Estradiol

In the corpus luteum no hormone other than progesterone has been discovered up to the present time.

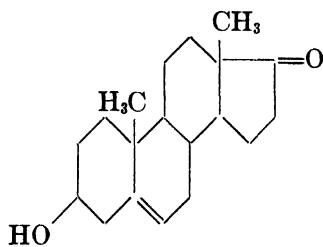
Androsterone has been isolated only from urine and not from testes. Detailed investigations in many laboratories showed that, while qualitatively the agreement in the physiological activity of androsterone and testicular extract was good, marked quantitative differences appeared. Particularly striking was the difference observed between the action of androsterone and testicular extract on the combs of capons on the one hand, and on the accessory sex glands of castrated rats on the other hand. Measured in terms of cock's comb units, equivalent doses of androsterone and testicular extract when given to castrated rats led to the observation that the testicular extract has several times the activity of androsterone on the accessory sex glands. As a consequence androsterone cannot be regarded as the principal testicular hormone.

Butenandt somewhat later succeeded in isolating from urine a second male hormone, dehydroandrosterone (VIII), which differs from androsterone in being unsaturated and in the spatial arrangement of the hydroxyl group on carbon 3. By the application of the sterol degradation method described for the synthesis of androsterone, it was possible in collaboration with Wettstein to complete the synthesis of this hormone. Investigators in other laboratories were also successful in preparing dehydroandrosterone by the same procedure. This method of degradation of sterols obviously has general application, since Marker and coworkers have applied it very recently for the preparation of estrone from a transformation product (VIIa) of ergosterol.



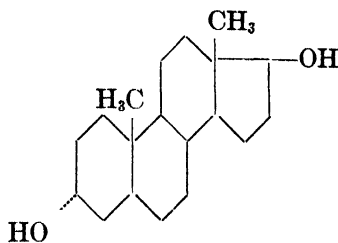
Dehydroandrosterone could not be responsible for the typical physiological action of the testicular extract since it has an activity less than androsterone. By hydrogenation, androsterone yields a diol (IX) the action of which on the cock's comb is about three times that of androsterone. Schematically, androstanediol can be compared to estradiol, but like androsterone and dehydroandrosterone it cannot be regarded as the

typical testicular hormone, since its action on the sex glands of rats is relatively feeble than that of androsterone.



VIII

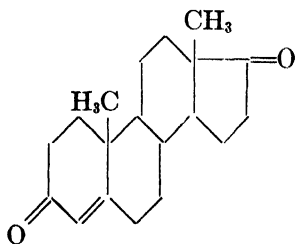
Dehydroandrosterone



IX

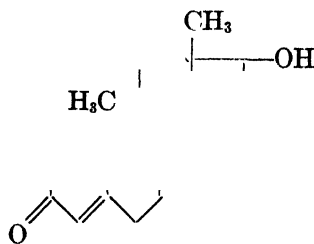
Androstanediol

In addition to the difference in physiological activity there is also a noteworthy difference in chemical behavior between all of the previously mentioned androstane derivatives on the one hand, and the testicular extract on the other. The male hormone activity of testicular extract could be destroyed by boiling with alkali, while androsterone and the other known androstane derivatives were stable under these conditions. On the assumption that the testicular hormone is a cholesterol derivative, it appeared to us probable that it contained an  $\alpha,\beta$ -unsaturated ketonic group, since such a linkage is relatively easily attacked by boiling alkali. The simplest compounds of this series analogous to androsterone are androstenedione (X) and androstenolone (XI).



X

Androstenedione



XI

Androstenolone

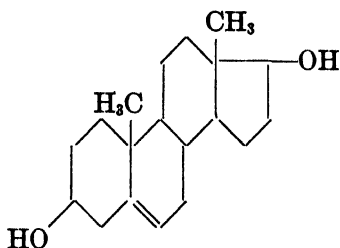
The problem as to whether either of these two compounds is the testicular hormone or not was investigated in collaboration with A. Wettstein and E. Tschopp. Androstenedione (X), prepared by the oxidation of dehydroandrosterone, had approximately the same physiological activity as androsterone as determined by the cock's comb test, but its action on the sexual glands of castrated rats was many times greater than that of androsterone. This gave the first experimental support to our hypothesis,

that the true testicular hormone might contain an  $\alpha,\beta$ -unsaturated linkage. It seemed very likely, therefore, that the second compound, androstenolone (XI), which contains a hydroxyl group in the 17-position, might have an increased activity and might be the testicular hormone that had previously escaped isolation. Androstenolone was thus prepared synthetically by a stepwise transformation of dehydroandrosterone.

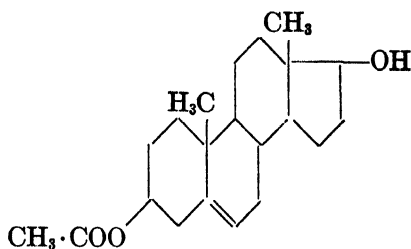
At this point, the synthetic approach to the problem coincided with the analytical procedure of Laqueur, David and their coworkers. These investigators succeeded in isolating a crystalline hormone from testes, which they named testosterone. This substance showed the same characteristic relationship between its action on the cock's comb and on the accessory sex glands as testicular extract. In view of the fact that androstenedione had shown the typical testicular hormonal action, David was led to attempt the oxidation of testosterone with chromic acid, and observed that the product obtained was identical with androstenedione. Simultaneously, it was possible to compare the synthetic androstenolone, prepared in our investigations, with testosterone. These proved to be identical and demonstrated the final proof of the structure of this important compound. During the same period Butenandt and Hanisch, while attempting to prepare new synthetic compounds with hormonal action, succeeded accidentally in obtaining testosterone by an exactly similar transformation.

As the yields of testosterone by the synthetic procedure were quite low, an improved method was sought and discovered in collaboration with Wettstein and Kägi. This permitted the production of testosterone on a large scale. Two essential improvements were developed. First, dehydroandrosterone was reduced to androstenediol (XII) with nickel and hydrogen without simultaneous reduction of the double bond. Second, two different ester groups were introduced in the 3- and 17-positions. Thus the monoacetate of dehydroandrosterone was reduced to the 3-monoacetate of androstenediol (XIII), and this substance was then benzoylated in position 17 (XIV). This made it possible to saponify the ester group in position 3 without affecting that in position 17. Partial saponification of the acetate-benzoate led to androstenediol 17-mono-benzoate (XV) in good yield, and this compound gave testosterone by oxidation and alkaline saponification.

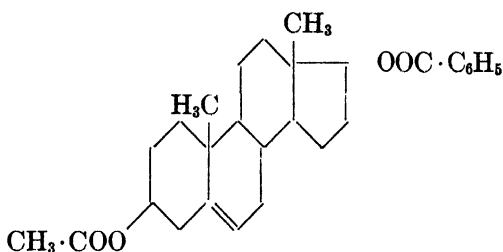
The close chemical relationship of the sex hormones introduces the question as to their origin in nature. Cholesterol might be considered as the single parent substance from which all of the sex hormones could be derived in a simple manner. The table on page 76 gives a hypothetical genesis of the sex hormones from cholesterol.



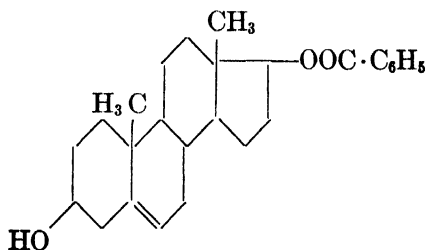
XII  
Androstenediol



XIII  
3-Acetate of androstenediol



XIV  
3-Acetate-17-benzoate  
of androstenediol

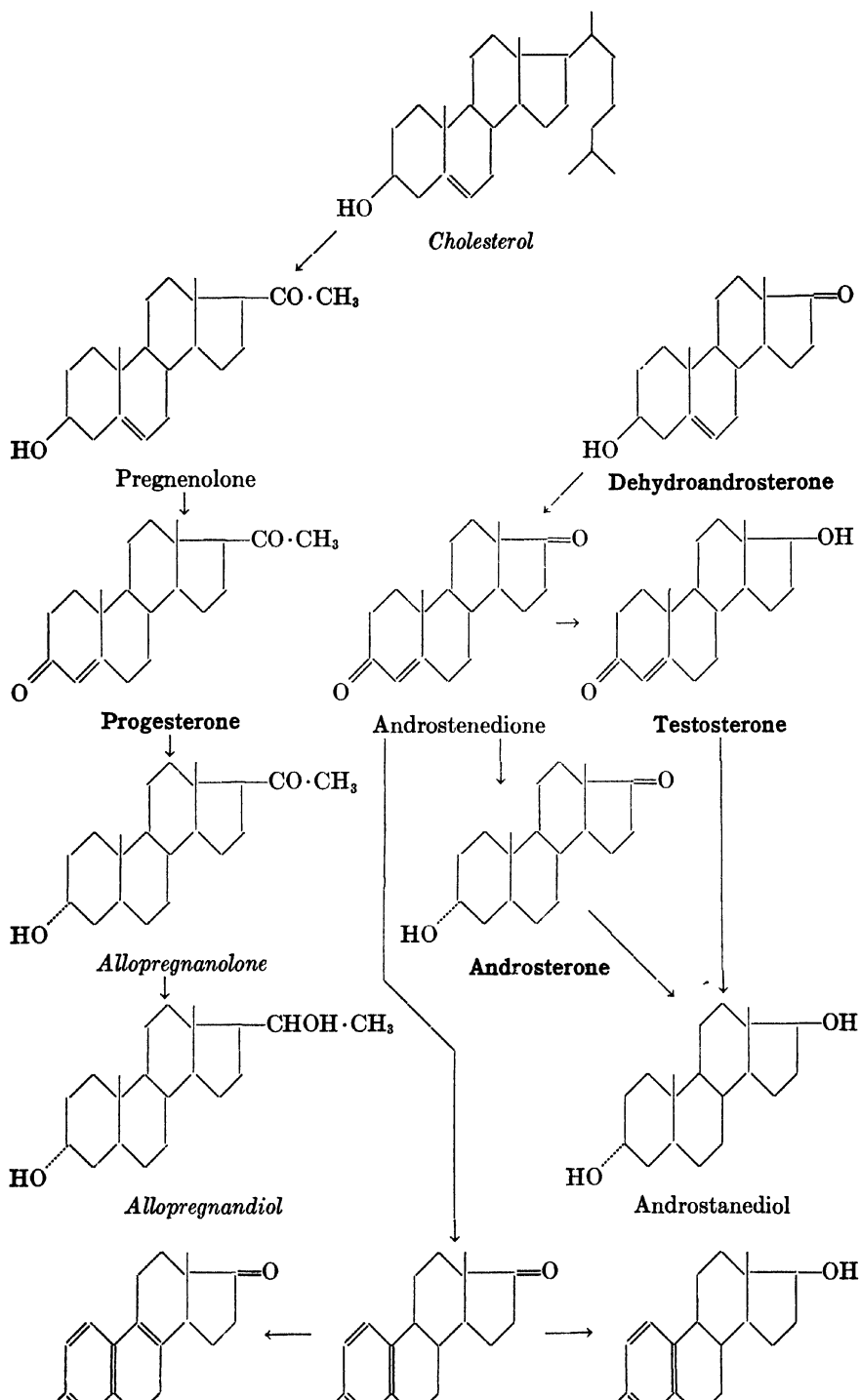


XV  
17-Benzoate of androstenediol

In the table, the hormones which occur in nature are printed in **bold-face type**, related compounds found in the organism but without hormonal action in *italics*, and compounds prepared synthetically but not yet found in nature in ordinary type.

Closest to cholesterol chemically are compounds of the progesterone group. These have not yet been prepared in the laboratory by the direct oxidation of a sterol. The stages of the assumed transformation in the pregnane and the androstane series are closely analogous (horizontal rows





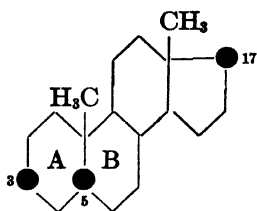
2 to 5 in the table). The first step may be the total or partial degradation of the side chain, resulting in the formation of the unsaturated ketones, pregnenolone and dehydroandrosterone. The second step may be the oxidation of the hydroxyl group in position 3 to a ketonic group. In the pregnane series the highest physiological activity is reached in the dike-tone, whereas in the androstane series the presence of the hydroxyl group in position 17 is essential for maximum activity.

It may be considered that the hormones of the estrane series are formed from an  $\alpha,\beta$ -unsaturated ketone of the androstane series by the loss of methane. Thus, for example, the ovarian hormone, estradiol, may be produced from the testicular hormone, testosterone. Equilenin, the most completely dehydrogenated derivative of the sex hormone series which has yet been found, may be considered as a dehydrogenated estrone. Whether nature follows such transformations as these is completely unknown and remains as a problem of the future.

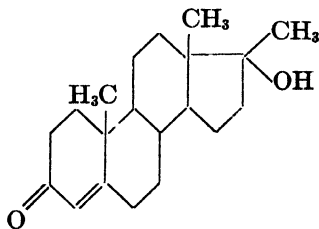
The relationship between physiological activity and chemical constitution in this general field is of unusual interest. Among the three groups of sex hormones, only in the androstane series is a relatively large number of synthetic and natural products which possess hormonal activity known. By slight chemical changes in progesterone, the activity is completely lost. In the case of estrone, the modifications of the molecule that are possible without disappearance of the activity are very limited.

Only the male sex hormones will be considered here, and in fact, it will be necessary to restrict the discussion to what appears now to be the most important of the physiological properties, namely the effect of the hormones in causing an increase in weight of the accessory sex glands of castrated rats. This property is of particular significance for the determination of the general and clinical value of the male hormones.

For the explanation of the results in the androstane series, the skeleton formula XVI is useful. The positions 3, 5, and 17 are specially designated, since changes in the molecule at these points are known to affect markedly the physiological properties. The differences between the various compounds thus far studied consist, first, in the spatial arrangement of the substituents at 3 and 5, second, in a modification of the functional groups at positions 3 and 17, and third, in the introduction of an olefinic linkage at carbon atom 5.



XVI



XVII

The introduction of a double bond at carbon atom 5 causes only a slight increase in activity. The spatial arrangement of the substituents at each of the three centers of asymmetry is of much more significance. The *trans* position of rings A and B, which involves the steric configuration of carbon atom 5, occurs in the cholestane series and is of decided importance for hormonal activity. The analogous *cis* compounds, the coprostane series, show no activity. The "normal" spatial configuration of the hydroxyl group in position 3, as is found in the naturally occurring sterols, leads to a definitely lower hormonal activity than the *epi* configuration, but the difference is not as marked as that caused by changing the steric configuration of rings A and B. The steric configuration of the hydroxyl group on carbon atom 17 as it exists in testosterone leads to a considerably higher activity than the opposite configuration. If the hydroxyl group in position 3 or 17 is converted to the corresponding keto group, the physiological activity of the resulting molecule is not materially affected.

The introduction of a tertiary alcoholic group in position 17 leads to an unexpected result: methyltestosterone (XVII) was approximately ten to twenty per cent more active than testosterone itself.

In this connection Laqueur and his collaborators have made the more important observation that the action of testosterone on the male accessory glands is increased about five times by the presence of a substance which could be isolated from testes or from other animal organs. This X-substance, which is a mixture, acid in character, has in itself no hormonal activity. Miescher, Wettstein, and Tschopp could increase the activity of testosterone when they added a higher fatty acid or hydroxy acid to the hormone solution which was to be injected. Palmitic acid, for example, was found to be particularly effective, but an amount considerably larger than that of the X-substance was necessary to achieve the same effect as the latter.

The highest physiological activity toward accessory sex glands has been found in recent researches by my collaborators Miescher, Wettstein, and Tschopp. A series of esters of testosterone has been carefully investigated. It has been observed that the formic, acetic, and propionic esters show approximately five times the activity of testosterone, or about the same activity as the mixture of testosterone and X-substance. The butyric and valeric esters show still higher activities, about ten times that of testosterone. A further increase in the molecular weight of the ester group results in a rapidly decreasing activity. Thus, for example, the palmitic ester has an extremely low activity in contrast to a mixture of palmitic acid and testosterone. The quantitative action of testosterone esters is not influenced by the addition of a fatty acid.

The high activity of the testosterone esters upon accessory sex glands is

even more surprising when a comparison is made with the activity upon the capon's comb. The most active esters show only one-fifth to one-tenth the activity of testosterone on the capon's comb. Using capon units as a fundamental comparative basis, the activity of the esters of testosterone on the accessory sex glands is nearly fifty times that of testosterone.

The discussion of hormonal action has been limited to animal experiments. It would be of greater interest to discuss the action of these substances on the human organism, but the evaluation of the physiological action of these substances on humans will require years before the knowledge is as complete as that which now exists for castrated rats.

The significance of hormones in the realm of nature may be touched upon briefly. What is a hormone? Do the many synthetic compounds whose male hormonal activity equals or even surpasses that of naturally occurring hormones, really deserve the name "hormones" or are they merely "pseudo-hormones"? The futility of such questions becomes apparent when it is considered that a whole series of synthetic male hormones, having a definite although small estrogenic activity, has been described. Moreover, Parkes has observed that some of these same compounds have a definite corpus luteum hormonal action. The physiological properties of a single hormone and the chemical nature of a group of hormones with similar physiological activity cannot be sharply defined.

The viewpoint of earlier investigators in the hormone and vitamin field that these substances are highly specific, is no longer tenable. Other numerous examples might be cited. Reichstein has synthesized a whole series of compounds possessing typical vitamin C action. Windaus has recently shown that natural vitamin D contains one double bond and one methyl group less than calciferol obtained by irradiating ergosterol.

How did the vitamins and hormones achieve their important place in nature? The hormones appear to be derived either from proteins or from cholesterol and can be considered as metabolic substances to which the organism has so accustomed itself that they have become indispensable to the normal progress of life processes. The vitamins may be defined as plant substances whose presence in the animal organism has also become absolutely necessary. It is to be emphasized that no causal connection exists between the origin of the hormones or vitamins and their final physiological function in the organism. Why should substances that have become important for life merely by accident be specific and irreplaceable?

In conclusion, it appears that the animal body during its gradual evolution has adapted itself to the hormones and to the vitamins, until these substances have become essential. That other chemical compounds may be found to replace them was consequently to be expected and has, during the last few years, been experimentally established.



# PROTEIN MOLECULES<sup>1</sup>

THE SVEDBERG

*Institute of Physical Chemistry, Upsala, Sweden*

*Received November 30, 1936*

Studies on protein solutions performed at the Institute of Physical Chemistry, Upsala, by means of sedimentation velocity and sedimentation equilibrium measurements in strong centrifugal fields (19, 20, 21, 22, 23, 24) as well as diffusion (33, 7) and electrophoresis (32, 10) determinations have brought to light a number of facts concerning the protein molecules. The main results of this work will be reviewed below.

Details of methods and apparatus have been given on previous occasions. The technique used may briefly be summarized as follows

## SEDIMENTATION VELOCITY MEASUREMENTS

A small quantity of the solution to be studied is vacuum-tightly enclosed in a small sectorial cell provided with plane-parallel quartz windows and rotated at constant (or but slightly changing) temperature in hydrogen at 20 mm. pressure. The main part of the machine—called the ultracentrifuge—is the chromium-nickel steel rotor (figure 1) designed on the principle of minimum strain. It is driven by means of two small oil turbines, one at each end of the (horizontal) shaft. To avoid vibrations the rotor journals move in special damping bearings. Speed measurement is accomplished through determining the period of an A.C. current generated by a magnetized zone of the rotor shaft acting on a soft iron-cored two-pole stator. The temperature of the cell is measured by means of a thermocouple attached to a small silver disc situated close to the rotor. Necessary temperature corrections are found by melting-point determinations in the cell. Figure 2 shows the ultracentrifuge with the lid raised, and figure 3 the work in an ultracentrifuge laboratory.

The resolving power of the ultracentrifuge is given by the expression  $\omega^2 x h$ , where  $\omega$  is the angular velocity,  $x$  the distance from the center of rotation, and  $h$  the height of the column of solution in the cell. High centrifugal force ( $\omega^2 x$ ) may be compensated, therefore, by high column of solution and *vice versa*. On grounds of rotor construction the maximum

<sup>1</sup> Presented at the Terecentenary Conference of Arts and Sciences, Harvard University, Cambridge, Massachusetts, September, 1936

value for  $\omega^2 rh$  attainable corresponds to a speed around 60,000 to 70,000 R.P.M., a rotor diameter of about 180 mm., and a height of column of solution of about 18 mm. Freedom from convection is essential for trustworthy measurements.

The process of sedimentation is followed (during rotation) by optical means. Two procedures of recording the sedimentation are used, viz., the light absorption method and the refractive index method. In the former pictures of the sedimenting column are taken from time to time by



FIG. 1 Recent rotor type with turbines and cell



FIG. 2. The ultracentrifuge with lid raised



FIG. 3. Ultracentrifuge laboratory

light of a wave length which the solute absorbs. In the latter method pictures of a finely ruled transparent scale are taken through the sedimenting column by light of a wave length which is not absorbed. The absorption method furnishes diagrams giving the relations between concentration ( $c$ ) of solute and distance ( $x$ ) from center of rotation. The diagrams of the refractive index method express the concentration gradient ( $dc/dx$ ) as a function of the distance from center of rotation. With the former method, therefore, each molecular species is brought out as a step

on the curve, while the latter one shows each molecular species as a maximum. The refractive index method is more accurate than the absorption method, especially for the analysis of mixtures, but it is much more laborious.

The sedimentation constant<sup>2</sup> ( $s$ ) is calculated from the formula

$$s = dx/dt \cdot 1/\omega^2 x \cdot \eta/\eta_0 \cdot \frac{1 - V\rho_0}{1 - V\rho} \quad (1)$$

where  $dx/dt$  is the observed sedimentation velocity,  $\eta$  and  $\eta_0$  the viscosities of solution and of water at 20°C.,  $V$  the partial specific volume of solute,  $\rho$  and  $\rho_0$  the densities of solution and of water at 20°C.

If the diffusion constant<sup>3</sup> ( $D$ ) of the solute is known, the molecular weight ( $M$ ) may be calculated from the expression

$$M = \frac{RTs}{D(1 - V\rho)} \quad (2)$$

where  $R$  is the gas constant and  $T$  the absolute temperature.

#### SEDIMENTATION EQUILIBRIUM MEASUREMENTS

In this case the shape of the cell is immaterial. A centrifugal force giving optimal concentration distribution has to be used. This force is, for a given substance, much lower than the force needed in sedimentation velocity determinations. The rotation has to be continued at constant temperature until test measurements have shown that equilibrium between sedimentation and diffusion is attained (this may take from a few days up to several weeks even for a column of solution not more than 5 mm. in height).

The molecular weight is computed from the equation

$$M = \frac{2RT \ln (c_2/c_1)}{(1 - V\rho)\omega^2(x_2^2 - x_1^2)} \quad (3)$$

where  $c_2$  and  $c_1$  are the concentrations at the distances  $x_2$  and  $x_1$  from the center of rotation.

#### DIFFUSION MEASUREMENTS

A cell with plane-parallel windows and provided with an arrangement for placing a column of solvent on top of a column of solution without disturbing the sharpness of the boundary is kept at strictly constant temperature. The change of concentration with time at the boundary between the two small—but from the point of view of diffusion—"infinitely"

<sup>2</sup> All sedimentation constants are expressed in units of  $10^{-13}$ .

<sup>3</sup> All diffusion constants are expressed in units of  $10^{-7}$ .



high columns of liquid is followed optically, preferably by means of the refractive index method. The diffusion constant ( $D$ ) is calculated from the following equation (or from formulas derived from it)

$$dn/dz = \frac{n_1 - n_0}{2\sqrt{\pi Dt}} \cdot e^{-z^2/4Dt} \quad (4)$$

where  $n_1$  and  $n_0$  are the refractive index of solution and solvent, respectively, and  $z$  is the distance from the original boundary. If the absorption method is used the diffusion constant is found from the following equations.

$$D = z^2/4y^2t \quad (5a)$$

$$c_s = c_0/2 \left( 1 - 2/\sqrt{\pi} \int_0^y e^{-y^2} dy \right) \quad (5b)$$

#### ELECTROPHORESIS MEASUREMENTS

In a quartz U-tube of good optical quality the solution to be studied is placed underneath the solvent and an electric potential gradient created over reversible electrodes. From observations on the movement of the boundary by means of the absorption or the refractive index method the electrophoretic mobility is derived. A plot of such data as a function of pH furnishes two important constants, viz., the isoelectric point and the mobility per pH unit in the isoelectric region.

The mass and shape of the protein molecule is perfectly well-defined in spite of the often enormous size. This means that the solution of a certain protein is either homogeneous with regard to molecular weight or contains a limited number of different molecular species (as a rule in equilibrium with each other). Mass and shape are defined by the environment (viz., pH., concentration of protein, concentration of salts and other solutes present) and respond stepwise by reversible dissociation-association reactions to changes brought about in the environment. These striking regularities justify, I think, the use of the term "molecule" for the protein particle.

In support of the above statements the following examples of measurements may be given.

If sedimentation proceeds so quickly that no appreciable diffusion takes place during a run (e.g., with high-molecular weight proteins) the molecular homogeneity is demonstrated simply by the sharpness of the receding boundary (figure 4).

An example of the behavior of a non-homogeneous high-molecular weight substance<sup>4</sup> is given in figure 5.

<sup>4</sup> Stanley's recent preparations, which have been made in a chemically milder way, are homogeneous.

If the sedimentation proceeds more slowly so that appreciable diffusion takes place during a run, the homogeneity can be tested by constructing the theoretical sedimentation-diffusion curves and comparing those with the observed ones (figure 6).

A still more severe test consists in calculating the apparent diffusion constant from a centrifuge run and comparing this value with the diffusion constant determined outside the centrifuge. In the case of an inhomogeneity with regard to molecular weight the former value will be higher than the latter because of the spreading of the boundary by the centrifugal field.

A homogeneity test may also be performed by means of sedimentation equilibrium measurements. The molecular weight values should be independent of distance from the center of rotation (figure 7).

A third method of testing the homogeneity consists in comparing the observed distribution of concentration in a diffusion determination with the theoretical ideal dispersion (figure 8).

As an example of the sedimentation analysis of a natural mixture of several proteins, figure 9 gives the diagrams obtained for cow's milk by means of the refractive index method.

The pH response of a protein is exemplified by the pH stability diagram of Helix hemocyanin given in figure 10. At the isoelectric point the protein contains only one component, but on lowering or raising the pH we arrive at points where a very small change in pH causes a great change in the molecular state. The original molecule ( $s = 98.9$ ; molecular weight 6,740,000) dissociates stepwise into halves ( $s = 62.0$ ), eighths ( $s = 16.0$ ), and sixteenths ( $s = 12.1$ ).

The products of pH dissociation represent perfectly homogeneous components, as demonstrated by figure 11.

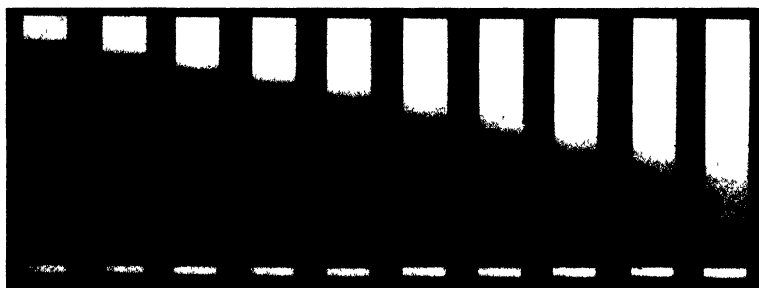
The reversibility of the pH influenced dissociation-association process is demonstrated by the following experiment. A solution of Helix hemocyanin at pH 6.8 of sedimentation constant 98.9 (molecular weight 6,740,000) was brought to pH 8.0, where it contains three components with the sedimentation constants 98.9, 62.0, and 16.0 (molecular weights 6,740,000, 3,370,000, and 842,000). The pH was then changed back to 6.8 and a sedimentation analysis performed. It was found that all the fragments of dissociation had completely united to form the original component of  $s = 98.9$  (molecular weight 6,740,000).

High dilution often causes dissociation. Thus hemoglobin upon dilution is partly split into half molecules (14). In a dilute solution of thyroglobulin there are present several dissociation products. The effect is favored by high pH and low salt concentration (figure 12).



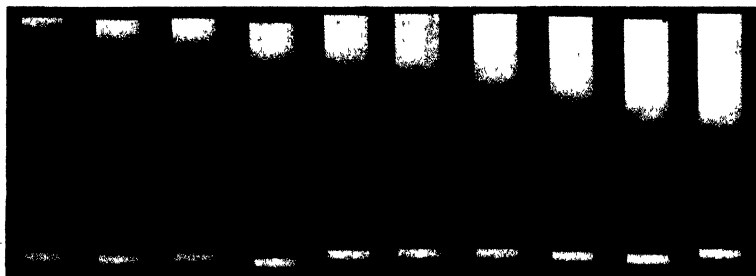
a

FIG. 4. Sedimentation pictures (a) obtained by means of the absorption method and curves of concentration distribution (b) for the hemocyanin from *Helix pomatia* at pH 5.5 ( $M = 6,740,000$ ;  $s = 98.9$ ; see footnote 2); centrifugal force 45,000 times gravity; time between exposures 5 minutes (I.-B. Eriksson-Quensel (2))



a

FIG. 5. Sedimentation pictures (a) obtained by means of the absorption method and curves of concentration distribution (b) for the tobacco mosaic virus protein at pH 6.8 (mean  $M = 17,000,000$ ;  $s = 236$ ); centrifugal force 15,000 times gravity; time between exposures 5 minutes (I. B. Eriksson-Quensel (4)). The virus protein is homogeneous in its native state and in preparations isolated in a chemically mild way.



a

FIG. 6. Sedimentation pictures (a) obtained by means of the absorption method and curves of concentration distribution (b) for  $\alpha$ -lactalbumin ( $M = 17,600$ ;  $s = 1.9$ ;  $D = 10.6$ ; see footnote 3); the observed curves and the theoretical values (points in the diagram) agree, showing that  $\alpha$ -lactalbumin is homogeneous with regard to molecular weight; centrifugal force 310,000 times gravity; time between exposures 40 minutes (K. O. Pedersen (11))

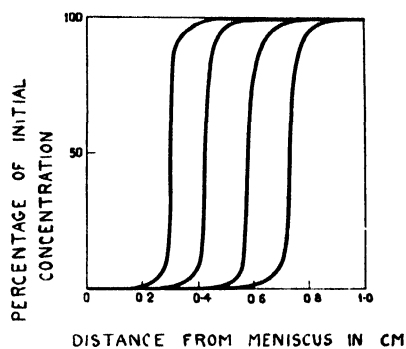


Fig. 4b

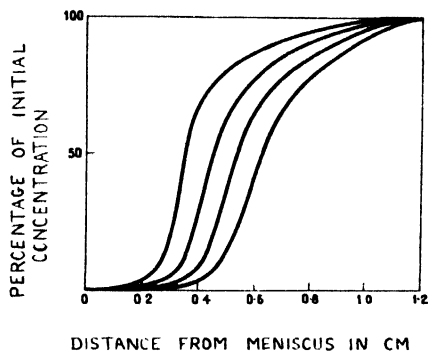


Fig 5b

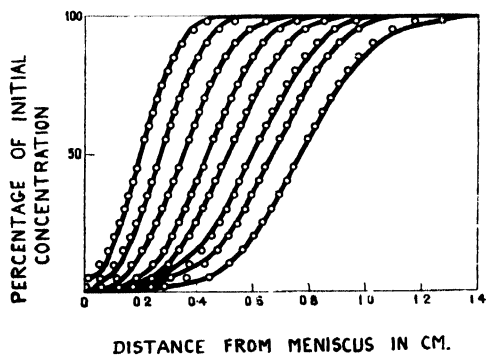


Fig 6b

Addition of an amino acid or of another protein often causes dissociation. Thus serum albumin may be split by adding clupein (figure 13).

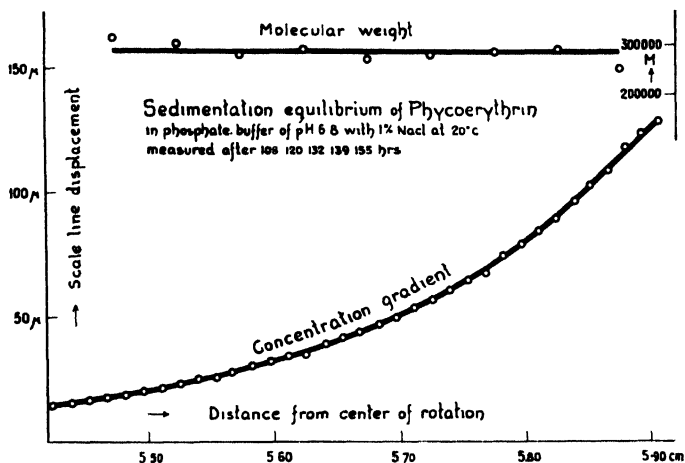


FIG. 7 Relation between molecular weight and distance from center of rotation for phycocerythrin ( $M = 281,000$ ) at pH 6.8; the constancy of molecular weight throughout the whole x-region demonstrates the homogeneity of this protein (I-B Eriksson-Quensel (3))

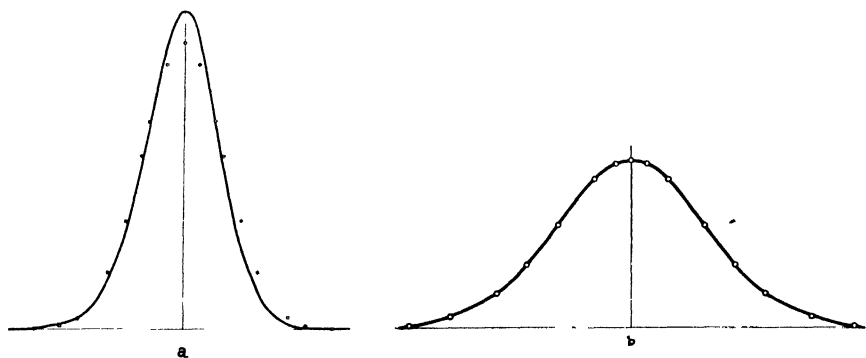


FIG. 8. Diffusion curves and ideal distribution points for crude gliadin (a) and for purified gliadin (b); the ideal form of the latter curve demonstrates the homogeneity of the substance ( $M = 27,000$ ;  $s = 2.10$ ;  $D = 6.72$ ) (O Lamm and A. Polson (7)).

A certain small amount of association product is formed together with the dissociation product when clupein is added to serum albumin. This is seen as a small maximum (C) ( $s = 7$ ) in figure 13a.

High salt concentration may cause dissociation or association. In

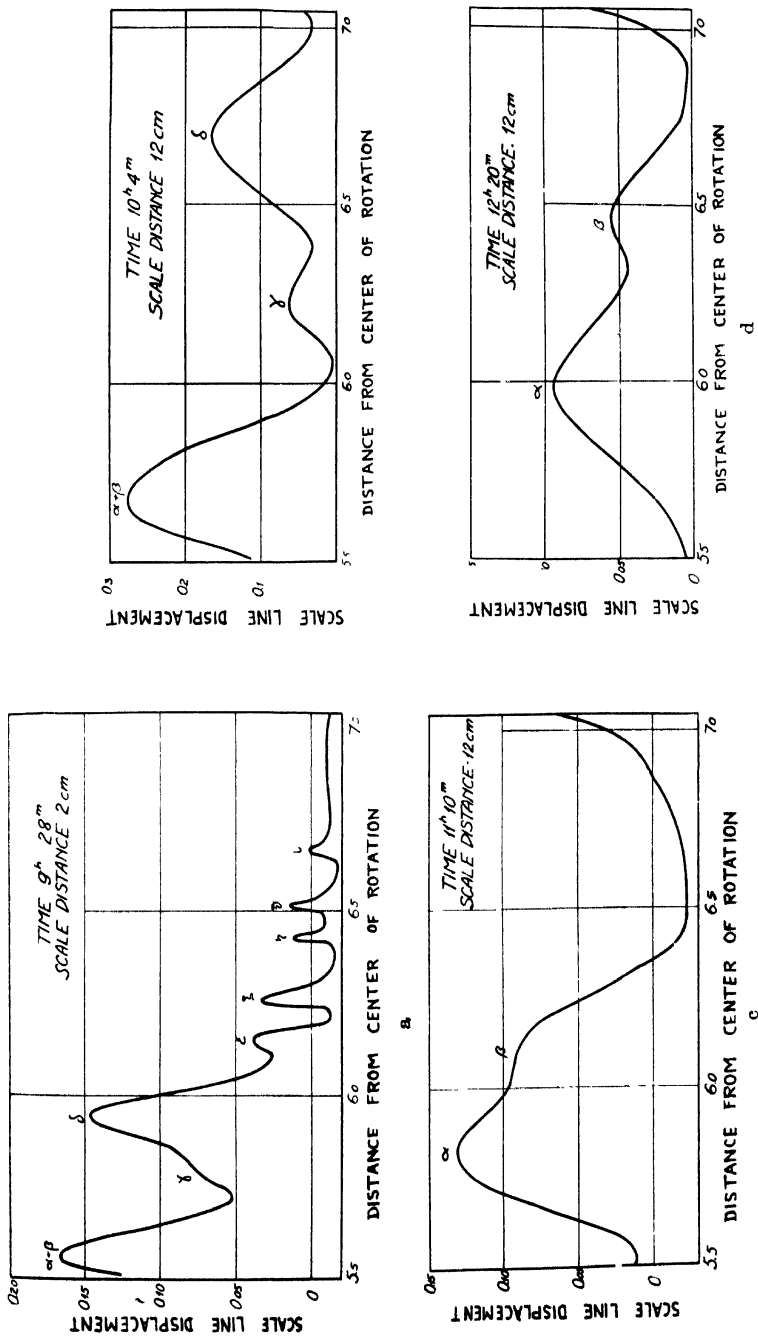


Fig. 9 Sedimentation curves for the proteins in cow's milk obtained by means of the refractive index method; (a) represents the state 13 minutes, (b) 49 minutes, (c) 115 minutes, and (d) 185 minutes after reaching full speed; in (a) no separation of the molecular species  $\alpha$  and  $\beta$  (lactalbumins) can be noticed,  $\gamma$  (lactoglobulin) is just visible as a hump on the curve,  $\delta$  (casein) has developed an incomplete maximum, and  $\epsilon$ ,  $\zeta$ ,  $\eta$ ,  $\theta$ ,  $i$  (caseins) are represented by separate maxima; in (b) the maximum  $\alpha + \beta$  begins to develop a dissymmetry,  $\gamma$  is clearly visible,  $\delta$  is well separated, and  $\epsilon$ ,  $\zeta$ ,  $\eta$ ,  $\theta$ ,  $i$  have sedimented down completely; in (c)  $\beta$  is seen as a hump on the curve,  $\delta$  and  $\gamma$  have sedimented down completely; in (d)  $\alpha$  and  $\beta$  are well separated (K. O. Pedersen (12)).

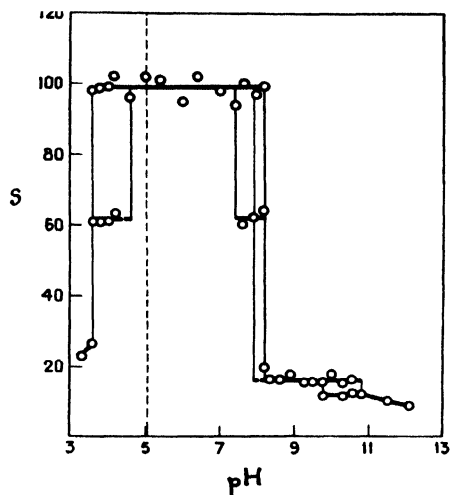
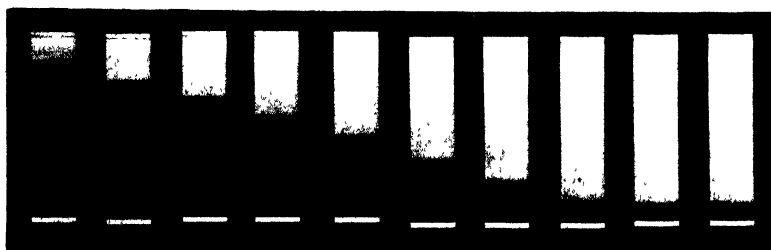
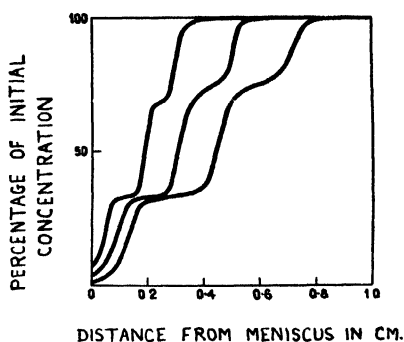


FIG. 10. The pH stability diagram for the hemocyanin from *Helix pomatia*. (I.-B. Eriksson-Quensel (2))

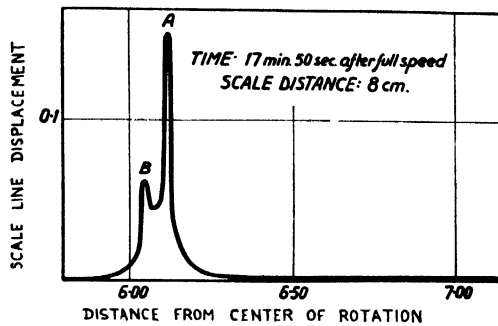


a

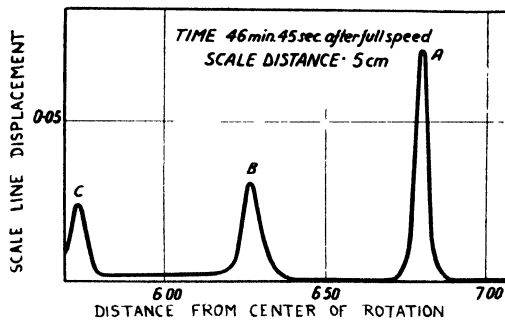


b

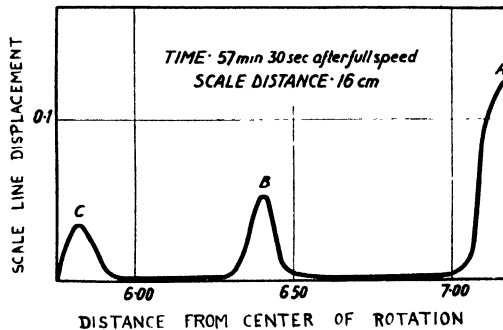
FIG. 11. Sedimentation pictures (a) obtained by means of the absorption method and curves of concentration distribution (b) for the hemocyanin from *Helix pomatia* at pH 8.2; molecular weight of components 6,740,000 ( $s = 98.9$ ), 3,370,000 ( $s = 62.0$ ), and 842,000 ( $s = 16.0$ ); centrifugal force 60,000 times gravity; time between exposures 5 minutes (I.-B. Eriksson-Quensel (2)).



a



b



c

FIG 12. Sedimentation diagrams of a thyroglobulin solution containing besides the normal thyroglobulin ( $s = 19.2$ ) two dissociation products ( $s = 10.1$  and  $6.3$ ) caused by prolonged action (fourteen days) of low protein concentration (0.09 per cent), low salt concentration (0.002  $M$  borate buffer), and high pH (10); centrifugal force 180,000 times gravity (H. Lundgren (8))



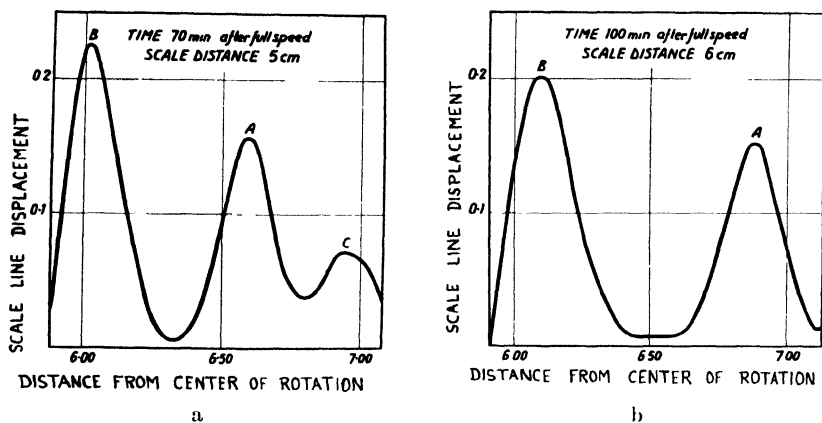
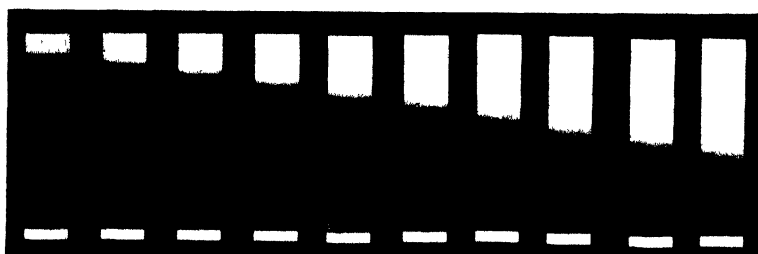
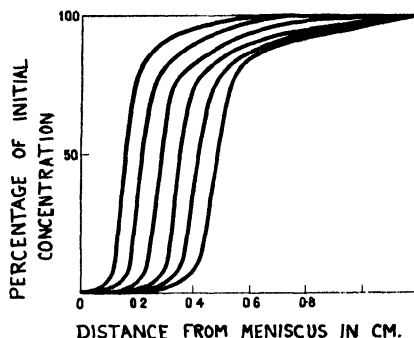


FIG. 13. Sedimentation diagram of serum albumin in 2.6 per cent clupein solution; the rapidly sedimenting maximum, A, represents undissociated protein, the slowly sedimenting maximum, B, is the dissociation product (sedimentation constant about 1 and molecular weight around 1/8 of that of serum albumin); the sedimentation of the clupein itself has been subtracted from the curves (K. O. Pedersen (13))



a



b

FIG. 14. Sedimentation pictures (a) and curves of concentration distribution (b) for normal thyroglobulin ( $M = 685,000$ ;  $s = 19.2$ ); centrifugal force 120,000 times gravity; time between exposures 5 minutes (H. Lundgren (8)).

solutions of thyroglobulin ( $s = 19.2$ ; molecular weight 685,000) the addition of 4 molar sodium chloride gives rise to a homogeneous association product of  $s = 196$ , corresponding to a molecular weight of about 16 million (figures 14 and 15).

A pure protein is perfectly homogeneous with regard to electrochemical behavior, as is borne out by electrophoretic measurements. Figure 16

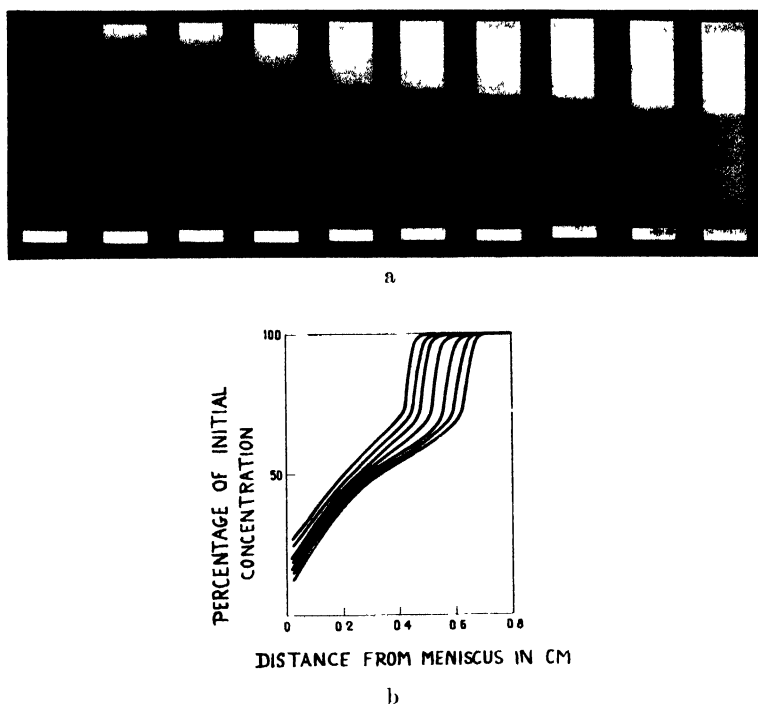


FIG 15 Sedimentation pictures (a) and concentration distribution (b) for thyroglobulin partly associated ( $M = 16$  million;  $s = 196$ ) by standing for twenty-three hours at  $5^{\circ}\text{C}$  in the presence of 4  $M$  sodium chloride; the thyroglobulin concentration was 0.05 per cent; the pH 4.8; centrifugal force 8800 times gravity; time between exposures 10 minutes (H. Lundgren (8))

shows the migration of *Helix* hemocyanin. In this case there is very little diffusion and curve 4, which is obtained after reversing the current, coincides with curve 1. No electrophoretic separation has occurred, and the protein is therefore electrochemically homogeneous.

Chemical inhomogeneity is easily revealed by electrophoresis measurements. Figure 17 shows the migration of leucosin. Here there is a marked spreading of the boundary from curve 1 to 2. On reversing the

current the separation is also reversed. The small difference between 1 and 3 is due to diffusion.

If the difference in isoelectric points between the components of a mixture is sufficiently large, steps appear on the curve. This is demonstrated by figure 18, which gives the migration of a mixture of phycoerythrin (isoelectric point 4.25) and c-phycoeyan (isoelectric point 4.76). During the time between curve 1 and curve 3 considerable separation has taken place. This is reversed when the current is commutated, so that curves 1 and 5 differ only by a small diffusion effect.

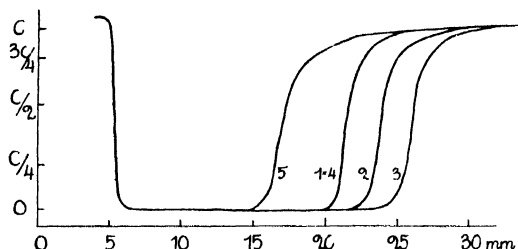


FIG. 16. Electrophoretic curves for the hemocyanin from *Helix pomatia* at pH 6.9 (A Tiselius (32))

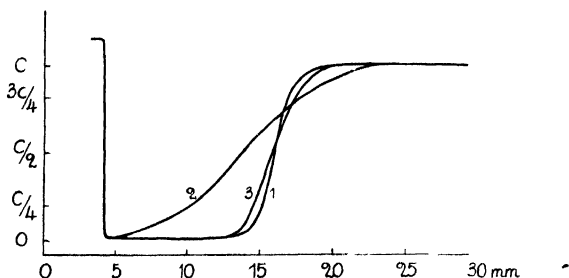


FIG. 17. Electrophoresis curves for leucosin (A Tiselius (32))

A protein solution may contain molecules of different mass and still be homogeneous in electrochemical respect. This means that it is a mixture of different states of aggregation of a chemically homogeneous substance. The well-defined components formed by a moderate pH change cannot be separated by electrophoresis (figure 19).

On the other hand a protein solution may contain molecules of the same mass but differing in electrochemical respect. This means a mixture of chemically different substances in the same state of aggregation.

As already pointed out, dissociation and association take place in large

steps and this gives rise to a relationship of simple multiples interconnecting the various molecular states of a certain protein. The masses of many protein molecules—even those belonging to chemically different substances—show a similar relationship. This remarkable regularity points to a common plan for the building up of the protein molecules. Certain amino acids may be exchanged for other ones and this may cause slight deviations from the rule of simple multiples, but on the whole only a very limited number of masses seem to be possible. Probably the protein molecule is built up by successive aggregation of definite units but

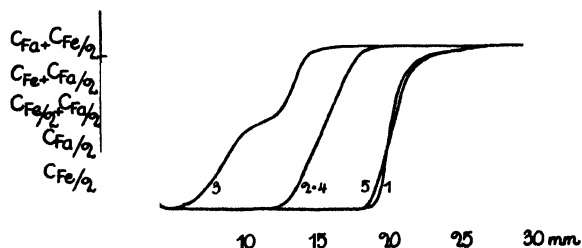


FIG. 18. Electrophoresis curves for a mixture of phycoerythrin and c-phyococyan (A. Tiselius (32))

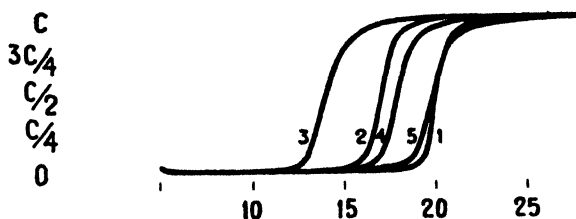


FIG. 19. Electrophoresis curves for the hemocyanin of *Helix pomatia* at pH 7.9. There is no separation, although the solution contains three components of molecular weight 6,740,000, 3,370,000, and 842,000 (K. O. Pedersen (11)).

in such a way that only a few aggregates are stable. The higher the molecular weight the fewer are the possibilities of stable aggregation. The steps between the existing molecules therefore become larger and larger as the weight increases. These statements are born out by table 1 in which are collected recent data for the various constants of protein molecules as determined in Upsala.

To sum up one may state that recent work has shown protein molecules to be better defined but also more labile than expected. The lability reveals itself in a number of well-defined and reversible dissociation-asso-

TABLE 1  
Various constants of protein molecules

PROTEIN	$\epsilon_{20}$	$D_{20}$	$M_s$	$M_v$	$M_{\text{calcd}}$	ISOLEUC- TRIC POINT	$\frac{du}{d\mu_2} \times 10^4$	REFERENCES
Erythrocrucrin ( <i>Lampetra</i> ) . . . . .	1.90	10.1	18,300	19,000	17,600 = $\frac{1}{2} \times 35,100$	5.60	3.2	(27, 16, 11)
Lactalbumin $\alpha$ . . . . .	1.9	10.6	17,300			5.12	6.7	(6, 16)
Cytochrom C . . . . .	1.89	10.13	15,600			9.7		(1, 31)
Erythrocrucrin ( <i>Arca</i> ) . . . . .	3.46			33,600	35,100			(27)
Erythrocrucrin ( <i>Chironomus</i> ) . . . . .	2.00			31,400		5.40	3.6	(27, 11)
Lactoglobulin . . . . .	3.12	7.25	42,000	37,900		5.19	11.9	(12, 17)
Pepsin . . . . .	3.3	9.00	35,500	39,200				(15, 16, 3)
Insulin . . . . .	3.47			35,100				(18)
Bence-Jones $\alpha$ . . . . .	3.55			35,000		5.20	5.8	(30, 32)
Bence-Jones $\beta$ . . . . .	2.85	7.33	37,600			5.46	3.5	(1, 16)
Egg albumin . . . . .	3.55	7.76	43,800	40,500		4.55	10.4	(11, 33)
CO-hemoglobin (horse) . . . . .	4.5	6.3	69,000	68,000	70,200 = $2 \times 35,100$	6.92	7.2	(33, 28)
CO-hemoglobin (man) . . . . .	4.5	6.9	63,000			7.09	6.4	(7, 11)
Serum albumin (horse) . . . . .	4.5	6.45	67,100	66,900		4.80	9.1	(9, 6, 7)
Yellow ferment . . . . .	5.76	6.28	82,800	77,900		5.22	6.4	(6, 16)
Serum globulin (horse) . . . . .	7.1			150,000	140,400 = $4 \times 35,100$			(9, 3)
Phycocyan ( <i>Ceranium</i> , dissociation compound) . . . . .	6.2			146,000		4.85	10.2	(3, 25, 11)
Phycocerythrin ( <i>Ceranium</i> ) . . . . .	12.0	4.00	290,000	292,000	281,000 = $8 \times 35,100$	4.25	14.2	(25, 33, 32)
Phycocyan ( <i>Ceranium</i> , main compound) . . . . .	11.4	4.05	272,000	276,000		4.85	10.2	(3, 25, 33, 11)
Edestin . . . . .	12.8	4.00	303,000					(16)
Excelsin . . . . .	13.3	4.26	294,000					(16)
Amandin . . . . .	12.5	3.62	329,000					(16)

Erythrocrutorin ( <i>Daphnia</i> ).....	16.3					421,200 = 12 × 35,100			(27)
Hemoecyanin ( <i>Pandatus</i> ).....	17.4				397,000				(2)
Hemoecyanin ( <i>Palaenurus</i> ).....	16.4	3.4	446,000		447,000				(2, 16)
Hemoecyanin ( <i>Helix pomatia</i> , dis- sociation compound).....	12.1	2.23	502,000				5.05	8.1	(2, 16, 32)
Hemoecyanin ( <i>Busycon</i> , dissocia- tion compound).....	13.5	3.29	379,600				4.49	10.7	(2, 16, 11)
Hemoecyanin ( <i>Eleidone</i> ).....	10.6	2.16	457,000				4.6	14	(2, 16, 11)
Thyroglobulin.....	19.2	2.39	696,000		675,000		4.58	11	(5, 16)
Hemoecyanin ( <i>Nephrops</i> ).....	24.5	2.79	812,000			842,000 = 24 × 35,100	4.64	13.3	(2, 16, 11)
Hemoecyanin ( <i>Homarus</i> ).....	22.6	2.78	752,000		803,000		4.95	18	(2, 16, 11)
Hemoecyanin ( <i>Helix pomatia</i> , dis- sociation compound).....	16.0	2.06	719,000		797,000		5.05	8.1	(2, 16, 32)
Hemoecyanin ( <i>Helix nemoralis</i> , dissociation compound).....	16.6	1.92	799,000				4.63	11.4	(2, 16, 10)
Erythrocrutorin ( <i>Planorbis</i> ).....	33.7	1.96	1,634,000		1,539,000	1,685,000 = 48 × 35,100	4.77	10.6	(27, 7, 10)
Hemoecyanin ( <i>Calocaris</i> ).....	34.0				1,329,000				(29, 2)
Hemoecyanin ( <i>Octopus</i> ).....	49.3	1.65	2,785,000			2,950,000 = 84 × 35,100	4.6	14	(2, 17)
Hemoecyanin ( <i>Eleidone</i> ).....	49.1	1.64	2,790,000						(2, 16, 11)
Erythrocrutorin ( <i>Arenicola</i> ).....	57.4				3,000,000	3,370,000 = 96 × 35,100	4.56	16	(26, 10)
Chlorocrutorin ( <i>Spirographis</i> ).....	55.2								(3)
Hemoecyanin ( <i>Rossia</i> ).....	56.2	1.58	3,316,000						(2, 16)
Erythrocrutorin ( <i>Lumbricus</i> ).....	60.9	1.78	3,190,000		2,946,000		5.28	12.6	(26, 16, 11)
Hemoecyanin ( <i>Helix pomatia</i> , main compound).....	98.9	1.38	6,630,000		6,680,000	6,740,000 = 192 × 35,100	5.05	8.1	(2, 16, 32)
Hemoecyanin ( <i>Busycon</i> , (main compound).....	101.7	1.38	6,814,000				4.49	10.7	(2, 16, 11)
Hemoecyanin ( <i>Busycon</i> , aggrega- tion compound).....	130.4	1.17	9,980,000			10,100,000 = 288 × 35,100	4.49	10.7	(2, 16, 11)

ciation reactions, the causes of which are changes in the environment. This fact opens up new possibilities for explaining the protein transport in the living organism.

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# MOLECULAR TRANSLATION, ROTATION, AND VIBRATION IN CHEMICAL ACTIVATION

O. OLDENBERG

*Research Laboratory of Physics, Harvard University, Cambridge, Massachusetts*

AND

A. A. FROST

*Department of Chemistry, Northwestern University, Evanston, Illinois*

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## I. INTRODUCTION

In recent years a large amount of work has been done concerning the transfer of energy among translation, rotation, or vibration in molecular collisions in gases. The experiments cover fields widely different from one another, i.e., spectroscopy, dispersion of sound, and rates of chemical reactions. The main purpose of the present review of these experiments is an attempt to derive general rules and to apply them to theories of gas reactions. In some chemical theories the energy of activated molecules is specified as vibration. Rotation and translation might also contribute energy towards activation. These kinds of energy have a limited lifetime, since they incur the risk of being dissipated by collisions. Hence their lifetime is measured not in seconds, as in the familiar case of excited atoms capable of spontaneous radiation, but instead in the total number



of collisions. In each individual case two questions ought to be answered: (1) Has the energy of activation a chance to survive intervening collisions until the assumed reaction takes place? (2) Is the collision process assumed for the reaction known to be more or less probable?

In this review we will neglect experimental technique as far as it is of no interest to the chemist. After a brief discussion of elementary processes that may produce molecules with a high energy of translation, rotation, or vibration, the results of the various experimental fields will be discussed: intensity distribution in band spectra as modified by pressure, dispersion of sound, rate of recombination of atoms in triple collisions, and activation of unimolecular reactions. While from these experiments direct evidence is derived on some processes and their probabilities, in the last section an attempt is made to apply these results to recent theories of gas reactions, in particular to the theory of energy chains in which a certain persistence of an activated molecule in collisions must be presupposed.

Recently a part of the same field was reviewed from the theoretical point of view by Zener (95). One cannot say that the quantum theory of collisions between atoms and molecules as yet gives a complete and accurate account of the facts. The more the theory approaches this aim, the more it seems worth while to review all related experimental evidence.

## II. ORIGIN OF ABNORMAL ENERGY OF TRANSLATION, ROTATION, OR VIBRATION

Before investigating what happens with high energy of translation, rotation, or vibration in collisions, we shall discuss the processes by which they may be produced. For the present we are not much interested in the study of thermal equilibrium, since in equilibrium the distribution of energy over translation, rotation, and vibration is maintained independent of the elementary processes responsible for the exchange of energy; in particular, independent of their persistence in collisions, so that lack of such persistence does not impair the reactivity. Instead, we shall study special processes that cause a deviation from the thermal distribution, a *small* deviation in high frequency sound or monomolecular reactions, and *very large* deviations in electric discharges or in some chemical reactions.

### *Translation and vibration*

We begin with processes in the electric discharge leading to high energy of translation or vibration. A fast electron is unable to give directly appreciable energy of translation to an atom or molecule. This is understood on the basis of the mechanical laws of impact applied to a collision

between a light and a heavy body. Nevertheless, it is well known that in the excitation process of a band spectrum (electronic excitation) a large amount of vibration can be produced. This is interpreted by the Franck-Condon rule as follows (75). In a molecule like  $I_2$  the nuclei have an equilibrium separation in the excited state widely different from that in the normal state. Suppose the molecule is excited by light or electron impact. During the excitation process proper, there is insufficient time for the heavy nuclei to change appreciably their separation, which is the equilibrium separation of the normal state. Hence an excited molecule is produced with its nuclei at the first moment far from the new equilibrium position. This molecule immediately begins to vibrate strongly. If this vibration exceeds a certain limit, the molecule dissociates and its constituent atoms or radicals might even fly apart with considerable energy as in the case of  $Cl_2$ . In this more indirect way, coupled with a dissociation process, an electron impact can produce energy of translation of the constituents far exceeding the thermal average.

But even without electronic excitation an electron with a few volt-electrons energy has a chance—in spite of its small mass—to impart vibration, for example, to a nitrogen molecule as was observed by Harries (28). Franck and Jordan (21) explain this apparent contradiction to the laws of impact as follows. From mechanics we learn that the electron cannot produce vibration by a knock on the nitrogen molecule in the direction of its axis, but mechanics is compatible with the following picture: the impinging electron penetrates the electronic structure of the molecule and by its field changes its equilibrium separation so that the molecule begins to vibrate. When the electron has passed the molecular structure, there is a chance that the molecule will continue to vibrate, the energy, of course, being provided by the electron.

In chemical changes it is obvious that the chemical energy might lead to high energies of translation, rotation, or vibration. Mulliken (55) observed, in particular, high vibration in band spectra excited by chemical processes.

### *Rotation*

The chances for producing high rotation, however, seem to be smaller than for high vibration, so much smaller, as a matter of fact, that in spectroscopy it is assumed as a rule—although a rather fallacious rule—that the rotation as observed in band spectra indicates the temperature of the gas. By electron impact no appreciable rotation can be given to a molecule. That is observed independently of whether or not the electronic system of the molecule is being excited. It is well explained by the laws of impact. In particular, the idea just applied to vibration as

excited by electron impact does not apply to rotation, since an impinging electron penetrating the electronic structure of a molecule cannot appreciably change its rotation, because its angular momentum with respect to the molecule is too small. For these reasons values of rotation far exceeding the thermal value, occasionally observed in band spectra, are called abnormal.

Elementary processes by which abnormal rotation of molecules may be produced have been discussed by Oldenberg (59, 60). They are related to the dissociation process in which the atoms fly apart with excess energy of translation. The most important process is the simultaneous excitation and dissociation of a complicated molecule, the fragments of which part from each other with considerable values of energy and possibly angular momentum, though the resulting angular momentum of the system remains small. This was first observed in the simultaneous excitation and dissociation of the  $\text{HC}\equiv\text{CH}$  molecule (53). The same type of process takes place in the electric discharge through water vapor when by electron impact the  $\text{H}_2\text{O}$  molecule is dissociated into H and excited OH, the OH being produced with high rotational energy. Rieke (71) recently proved that the excitation of  $\text{HgH}$  molecules by impacts of the second kind with metastable mercury atoms is a similar process (see section III B).

But it is obvious that in general only a part of the available energy goes into the rotation of a molecule. From this consideration and, in particular, from the spectroscopic fact that abnormal rotation is an exceptional case, we infer that vibration of molecules is much more important than rotation in representing energy of activation.

### III. THE LIFETIME OF HIGH ENERGY OF TRANSLATION, ROTATION, OR VIBRATION IN COLLISIONS

#### *A. Classical mechanics and energy of translation*

Since translation, rotation, and vibration of molecules are concerned with the motion of masses much heavier than electrons, it is supposed that classical mechanics describes collision processes within a certain approximation. A well-known example of the approximate validity of classical physics in describing the motion of nuclei is the Franck-Condon rule dealing with the intensity of band spectra discussed in the preceding section. Hence our discussion must start from classical physics. Conclusions derived from classical physics are as follows. Exchange of energy generally takes place in each collision process, particularly between particles of comparable mass. If one particle has an exceptionally large amount of energy, there is a tendency towards distribution over all degrees of freedom available, that is, towards thermal equilibrium. On the other

hand, it rarely happens that in a collision the energies of different degrees of freedom accumulate and so create abnormal energy in one degree of freedom. It follows that translation has a chance to activate a chemical reaction only if the atom or radical, somehow produced with high energy of translation, reacts without many intervening collisions.

The progress towards thermal equilibrium, however, is slowed down in collisions between very light and very heavy atoms, for scarcely any exchange of energy takes place. A striking example for an extreme case of this type of collision is given by the enormous selective temperatures of free electrons in electric discharges through gases which as a whole do not show much more than room temperature. This phenomenon, discovered in 1925 by Langmuir (51), is partly explained as follows: the free electrons receive large amounts of energy not from thermal collisions but from the electric fields. In their frequent collisions *with atoms* they change their direction and any loss of energy is slight. In their *mutual* collisions, however, an exchange of energy takes place so easily that a separate Maxwell distribution among the electrons is established with an average energy of several volt-electrons, many hundred times surpassing the thermal energy of the gas molecules.

On the other hand, positive ions when accelerated by the electric field lose their energy readily to atoms and so raise the temperature of the gas. This may be observed by the width of spectral lines emitted from ions. They fail to indicate by Doppler broadening higher velocities for ions than for atoms.

Apart from the short life of abnormal translation, the ability of translation to activate chemical reactions is still further restricted by classical mechanics. This will be evident from an example (22). In the photochemical chlorine-hydrogen combination the light absorbed generates chlorine atoms which may well have kinetic energy as high as 0.6 volt. But in the collision of a fast chlorine atom with a hydrogen molecule only a small fraction of this energy is available for activating the reaction since the common center of gravity, largely determined by the heavy chlorine atom, is sure to continue its path. The same restriction ought to be taken into account, for example, in a chain reaction, suggested by Semenov (35), in which one of the links consists of the dissociation of a hydrogen molecule by a fast hydrogen atom. Again the total kinetic energy is not available for the dissociation process. This restriction in the ability to activate reactions obviously does not apply to light atoms or molecules (in the extreme case electrons) when colliding with heavy ones.

In the transfer of vibrational or rotational energy of molecules in collisions similar restrictions may be explained by the laws of conservation of

energy and momentum (58). The effect of rotation on chemical activation was discussed by Beutler and Rabinowitsch (4) on the basis of classical physics.

Although classical physics represents molecular processes, if at all, only by an approximation, the results discussed are of practical value, as it is certain that restrictions derived from the conservation of energy and momentum really hold. It is uncertain whether additional restrictions come in by the laws of quantization. This is to be decided by experiments which will be discussed in subsequent sections.

### *B. Intensity distribution in band spectra*

In band spectra the vibration and rotation of molecules emitting light are directly observed. In excited molecules we are able to produce selective values of vibration and rotation and change them by collisions during the lifetime of the excited state. Here we have an outstanding opportunity to study the persistence of vibration and rotation. First we shall discuss fluorescence experiments in which the processes can be particularly well analyzed, and subsequently electric discharges.

1. *Fluorescence experiments.* The best known case is that of the fluorescence radiation of iodine vapor excited by monochromatic light, for example, the green mercury line. This spectrum was discovered by R. W. Wood (92). It consists of a long series, called resonance series, of very narrow doublets extending from the exciting green line through the yellow and red, representing a small selection of lines from the very complicated  $I_2$  bands. This series was interpreted by Lenz (52) and in greater detail by Loomis (54) as follows: the green mercury line coincides with one individual sharp absorption line of the iodine band spectrum, hence it affects only molecules with definite values of rotation and vibration. It produces molecules with a certain electronic excitation and in addition 26 vibrational and 34 rotational quanta, or with energies of vibration of 0.64 volt-electron and of rotation of 0.004 volt-electron. While this rotation is within the thermal range, the vibration represents 75 per cent of the energy of dissociation of the excited electronic level. At low pressure (0.2 mm.) this excited state represents the sole initial state of the radiation process observed as fluorescence. In radiation the electronic state goes down to the normal level as there are no other levels available. This determines the situation of the spectrum in the visible. In the same radiation process the *vibration* goes over to any vibrational quantum number of the normal electronic level, as no selection rule restricts the change of vibration. These various possible changes are observed as the resonance series of nearly equidistant "lines," indicating by their mutual distances the vibrational sublevels of the normal electronic level. Again

in the same process the *rotation* changes its quantum number by  $+$  or  $-$  unity according to the selection rule. These two possible changes—associated in the radiation process with any change of electronic level and vibration—can be observed only with high resolving power as a splitting up into fine doublets of all the vibrational “lines” just described. Thus we understand the main aspect of the fluorescence spectrum of  $I_2$  at low pressure, the resonance series, each “line” consisting of a narrow doublet.

We are particularly interested in the change produced in this series by the addition of a foreign gas to the iodine vapor. In this case a much larger variety of lines (a larger selection from the complete  $I_2$  bands) appears, as discovered by Franck and Wood (23). This is explained by collisions which during the lifetime of the excited state change its vibration or rotation. These new lines indicate by their intensities the probabilities for the transfer of vibrational or rotational energy. The intensities as functions of pressure have recently been determined by Roessler (11, 73) with photographic photometry. His chief result is that the probability for the transfer of vibrational as well as rotational energy from an excited iodine molecule to a colliding rare gas atom is of the order of magnitude one. The *vibration*, starting from a value far exceeding the thermal average, is never increased by collisions but reduced preferably by one quantum. The *rotation*, starting from a value within the thermal average, may gain as well as lose energy, readily changing by several quanta which are exceedingly small. Roessler describes in detail how this probability varies as a function of the atomic weight of the rare gas, uniformly increasing for vibration but with a certain maximum for rotation. The absolute values of probability are not so well known, since their determination depends upon a reasonable choice of the lifetime of the excited state and the cross sections. The numerical values given by Roessler indicate effective cross sections for the transfer of vibrational or rotational energy even larger than the gas kinetic cross sections.

While these quantitative results of photographic photometry indicate an easy exchange of rotation and vibration of the iodine molecules when excited by green light, an apparently contradictory result was obtained by Oldenberg (56) in the fluorescence radiation excited by ultra-violet light (2100–1849 Å. U.). These experiments were recently extended by Duschinsky, Hirschlaff, and Pringsheim (10) with higher resolving power and wider ranges of temperature, pressure, and wave length. The same type of resonance series starting from the wave length of the exciting line is observed. A great difference, however, is that for long wave lengths even at the lowest pressure (no collisions during the lifetime) the resonance series gradually goes over into a much more complicated “tail.” We are interested in that with increasing pressure of foreign gases the resonance

series loses intensity in favor of the "tail," but, strangely, within the series no new lines come out, not even in two atmospheres of nitrogen. This failure to observe a change of vibration or rotation is probably connected with recent results of Cordes (9), who proved the occurrence of predissociation in the iodine molecule. This would materially reduce the lifetime of the excited state below the value due to spontaneous radiation. Furthermore, collisions may induce predissociation rather than changes of vibration or rotation so that they remove excited molecules rather than change their vibration or rotation. For the purpose of this review we conclude that we are justified in discarding the ultra-violet iodine bands from our consideration, because the processes we are interested in are masked by other effects of collisions.

Another opportunity of investigating the lifetime of vibration and rotation is given by abnormally high values of rotation in certain fluorescence experiments and in electric discharges. As discussed in section II, some rather special processes are alone capable of producing abnormal rotation.

The first striking case was discovered by Wood and Gaviola (25, 93) in the fluorescence radiation of  $\text{HgH}$ , observed in the mixture of very little mercury vapor and hydrogen with a few centimeters of nitrogen. Illumination with the resonance line 2537 of mercury excites  $\text{HgH}$  bands with a rotation indicating an apparent temperature of many thousand degrees, although the experiment is performed at room temperature. An interpretation was offered by Oldenberg (58) and recently experimentally confirmed by Rieke (71). His results are as follows. In the rather complicated sequence of processes,  $\text{HgH}$  molecules (excited by impact of the second kind with excited  $\text{Hg}$ ) are produced with considerable excess vibration. This is a common process (described for electron impact by the Franck-Condon rule, section II). We are interested in how these vibrating molecules behave in collisions during the lifetime of the excited state, that is, how the spectrum changes with increasing pressure. These molecules when colliding with nitrogen have a good chance to transfer part of their excess vibrational energy into rotation, but a very poor chance to transfer it into translation. The reason is that before the collision the vibration consists largely of the motion of a light particle, the hydrogen atom, so that—according to classical mechanics (cf. section III A)—in the collision the translation, belonging to heavy particles ( $\text{HgH}$  and  $\text{N}_2$ ), scarcely receives energy and most of it remains concentrated in the degrees of freedom of the light particle; that is, in the hydrogen atom which is vibrating and rotating with respect to the mercury. In another paper Rieke (72) discusses an apparent persistence of rotational energy of  $\text{HgH}$  in its normal state in collisions as claimed several years earlier by Beutler and Rabinowitsch (5). Extreme intensity of the light

exciting fluorescence brings out some abnormal rotation in the HgH band. It is probably explained not by persistence of rotation but more indirectly by persistence of vibration from one excitation process (followed by radiation) to the next process. The vibration may change in collisions to the observed rotation. From these experiments, no quantitative results can be derived as from the fluorescence radiation of  $I_2$ , since the mean time between consecutive excitation-radiation processes is not known.

2. *Electric discharges.* While in fluorescence experiments the elementary processes can be traced in great detail as was done in particular by Rieke, similar phenomena in electric discharges are largely explained by analogy.

In the band spectrum of hydrogen to which a few millimeters of helium are added abnormal rotation was discovered by Richardson (70) and further investigated by Roy (74). N. D. Smith (81) traced its origin to a process similar to the one discussed for HgH. Excitation by electron impact readily leads to high vibration but normal rotation of the excited molecule (section II). If a few collisions with helium take place during the lifetime, the energy of vibration is dissipated over all degrees of freedom available; a small share goes into rotation of the same excited hydrogen molecule and becomes manifest at the radiation process. In this case (all masses about equal, different from the case  $HgH + N_2$ ), according to classical mechanics, translation ought to have the same chance to benefit as rotation. Since the vibrational energy which is to be distributed might easily be 1 volt and the average thermal rotation is only about one-fortieth of this value, a small fraction of the vibration dissipated may produce an appreciable gain of the rotation kept in the same molecule. Actually the abnormal rotation observed is much less conspicuous than in the HgH experiment. This case is unusual in that both the loss of vibration and the simultaneous gain of part of the energy as rotation can well be traced in the band spectrum. For higher pressure of helium the abnormal rotation goes back towards its normal value, indicating a more complete dissipation of energy by collisions taking place during the lifetime. This experiment proves that there is no very conspicuous persistence of vibration or rotation of excited  $H_2$  in collisions with He. But an appreciable persistence is observed at liquid air temperature. In this case, in spite of the addition of 200 mm. of helium to 0.6 mm. of hydrogen the rotation did not quite go down to the very low thermal average. The exchange between vibration, rotation, and translation seems to be slower than would be explained by the smaller number of collisions per second. An attempt to obtain quantitative results with photographic photometry seems well worth while.

At room temperature OH radicals behave similarly to hydrogen mole-



cules (59). Their abnormal rotation, excited in the discharge through water (section II), can well be dissipated during the lifetime of the excited state by collisions with helium, indicating no conspicuous persistence of rotation. It is striking that argon seems to have about the same effect in reducing the rotation of OH (64), although because of its larger mass, according to classical physics, one would expect it to have less chance to receive energy from the light hydrogen atom rotating about the oxygen atom.<sup>1</sup>

A remarkable persistence of vibrational energy in the normal state of  $H_2$  has been inferred by Beutler (3). In a discussion of intensities in an electric discharge through 0.02 mm. of hydrogen + 0.3 mm. of argon he assumes that an argon line is absorbed by  $H_2$ , although only hydrogen molecules in their normal electronic state with the vibrational quantum number  $v'' = 2$  (1.00 volt-electron) are able to absorb this line. It is obvious that such vibration cannot have thermal origin but must be a residue of preceding excitation and radiation processes. Hence it must be assumed that the first few vibrational quanta of the hydrogen molecule outlast many collisions.

In the electric discharge through nitric oxide E. Kondratjewa and V. Kondratjew (48) discovered that addition of argon transfers a vibrational quantum of excited nitric oxide (energy of quantum 0.126 electron-volt) with a probability of the order of unity.

Surveying the results of band spectra presented here, we emphasize the fact that many of them apply to excited electronic levels (fluorescence of  $I_2$  or  $HgH$ , spectra of  $H_2$  or OH in discharges) so that their application to the normal levels, more interesting in chemical reactions, may be questioned. On the other hand, some results derived from band spectra for normal levels (fluorescence of  $HgH$  at highest intensity, discharge through  $H_2 + Ar$ ) are only qualitative as the "time between consecutive excitation processes" is an unknown factor.

Persistence of vibration or rotation in collisions seems to be more pronounced the larger the individual quantum is as compared to  $kT$ . For example, the  $H_2$  rotation seems to become more persistent in collisions the lower the temperature (see section III G).

<sup>1</sup> From these results—interpreting abnormal rotation in electric discharges—one infers that some surprisingly high temperatures, recently observed (27, 31) by the rotational distribution of intensities in band spectra, might be due to collisions of highly vibrating molecules during the lifetime of the excited state and so fail to indicate the real temperature of the gas unless the experiments are carried through at a very low pressure.

### *C. Dispersion of sound*

1. *Fundamental experiments.* Dispersion of sound was discovered by G. W. Pierce (63) in 1925. He devised the accurate method for the measurement of the velocity of sound that has been applied in all later work, the source of sound consisting of a piezo quartz oscillator, the frequency of which can be very accurately measured and kept constant. Dispersion of sound is observed almost exclusively far above the audible range. Absorption of sound occurs in the same frequency range as dispersion.

In the theoretical interpretation it is important to note that dispersion of sound has been observed only for molecules with excited vibration. This holds at room temperature for carbon dioxide, chlorine, nitrous oxide, ammonia (84), and, to a smaller extent for oxygen, at higher temperatures for nitrogen. (From specific heat measurements (17) it is known that at room temperature vibration is not excited in hydrogen and nitrogen. This agrees with the fact derived from band spectra that the vibrational quanta of these gases are too large to be excited at room temperature by thermal collisions.) Dispersion is observed only within a limited range of high frequencies above and below which the velocity has constant but different values. Below this range the familiar value of velocity of sound is interpreted, following Einstein's theory of specific heats, by the idea that for chlorine, for example, translation and rotation are active as for any other diatomic molecule at room temperature, but that the vibration is only partly excited, as is to be expected from the value of its quantum as compared to  $kT$ . But above the critical range, the velocity of sound approaches the same higher value which in other gases (hydrogen) indicates that the vibration has no share in the specific heat although, of course, in chlorine the thermal excitation of vibration still ought to occur.

2. *Theory.* Herzfeld and F. O. Rice (32) give the following explanation. The vibration is inherently slow in picking up the energy value that belongs to thermal equilibrium, so that for very rapid changes of temperature, as they occur in high frequency sound, the energy content of vibration might fail to follow and instead persist at some average value determined by the average temperature. If so, the vibration loses its ability to affect the velocity of sound.

By the mathematical treatment of this idea, using the observed values of pressure, temperature, and the frequency range of dispersion, one can derive the average number of collisions required to produce exchange of energy between vibration and the other degrees of freedom (40, 44). This is the problem of the present review.

*Rotation* of molecules does not seem to persist through a sufficient

number of collisions to result in the dispersion of sound in the accessible frequency range (16, 69).

3. *Effect of impurities.* A discovery by Knudsen (46), who investigated absorption instead of dispersion of sound, gives a variety of experimental results and these are of greater importance to chemistry. He found that the critical frequency is very sensitive to certain impurities; for example, traces of water will shift it to higher frequencies (79). Such impurities as helium, for example, do not manifest dispersion of sound in themselves.

The explanation, consistent with the theory of Herzfeld and Rice, was given by Kneser (42, 43, 45). Although chlorine molecules are slow in exchanging vibrational energy in collisions among themselves, they accomplish this exchange readily in collision with water or with certain other molecules. In the more detailed theory given by Kneser, the critical frequency of dispersion leads to the number of collisions required on the average for the chlorine molecule to give its vibration to one or the other foreign atom or molecule.<sup>2</sup>

4. *Survey of results.* By the systematic investigation of dispersion of sound as it is affected by impurities Eucken (13) and his collaborators succeeded in establishing general rules for the lifetime of vibrations in collisions between various partners. Experimental results are given in table 1.<sup>3</sup>

An increase of temperature materially decreases the number of collisions required to dissipate one quantum. For chlorine, for example, this number decreases to one-seventh for an increase of temperature between  $-32^{\circ}$  and  $+145^{\circ}\text{C}$ .

5. *General conclusions.* From table 1 it is evident that the exchange between the vibrations of chlorine, nitrous oxide, or carbon dioxide in collisions with other molecules or atoms fails to follow a simple law, as a function of molecular weight. From the wide range of figures given in table 1 Eucken and Becker (15) derived a general law which is particularly striking when we compare the effect on chlorine of nitrogen and carbon monoxide as impurities, both molecules having the same weight and very similar physical properties (band spectra) but very different reactivity with chlorine. Nitrogen, which does not chemically react with chlorine, exchanges its vibration with chlorine once in 43,000 collisions, whereas for carbon monoxide, which under different conditions would react with

<sup>2</sup> A unique result has been derived by Kneser (41) from the measurements of Knudsen. When the vibration of  $\text{O}_2$  is dissipated by  $\text{H}_2\text{O}$ , triple collisions  $\text{O}_2 + \text{H}_2\text{O} + \text{H}_2\text{O}$  seem to play an appreciable part.

<sup>3</sup> Attention is called to the conventional representation of results of dispersion of sound based on the "number of collisions required to dissipate one quantum." This is reciprocal to the "yield per collision" applied in table 2.

chlorine to form phosgene, the corresponding ratio is only 1/230. Here evidently the effects of the foreign gases on the dispersion of sound in chlorine correspond to their chemical reactivity.

Similar results, characteristic for certain combinations, led Franck and Eucken (20) to the idea that the mechanical picture of exciting, or dissipating, vibration by a knock on one of the chlorine atoms fails, that instead an interaction must be assumed between the electronic structure of the two colliding molecules similar to the beginning of a chemical reaction. We shall discuss the gain of vibrational energy which is a problem equivalent to its loss. We compare the excitation of vibration in a molecule by collision with another molecule with the effect of an electron impact exciting vibration as discussed in section II. The close approach of another

TABLE 1

*Number of collisions required to dissipate one quantum of vibration (20°C.)*

ADDED GAS	PRINCIPAL GAS		
	Cl <sub>2</sub>	N <sub>2</sub> O	CO <sub>2</sub>
No added gas . . . . .	34000	5600	47000
N <sub>2</sub> . . . . .	43000		
A . . . . .	32000		47000
He . . . . .	900	1700	1700
D <sub>2</sub> . . . . .		440	
H <sub>2</sub> . . . . .	780	630	480
CO . . . . .	230	3600	
CH <sub>4</sub> . . . . .	190	840	2400
HCl . . . . .	120		130
NH <sub>3</sub> . . . . .		450	
H <sub>2</sub> O . . . . .		60	40
CO <sub>2</sub> . . . . .		5000	

molecule ought to change the molecular forces. It might start a vibration which would have a chance to persist when the two colliding molecules part again. Such an interaction is obviously not determined just by the masses,—as the mechanical knock probably would be. Instead it is characteristic for the individual pair of molecules.

Thus the following rule given by Eucken and Becker (15) is understood: the probability of a transfer of vibration in a collision is larger, the larger the chemical affinity between the partners, although here actually no chemical reaction takes place. Eucken (13) emphasized that in particular chemical reactions with small heats of activation ought to manifest themselves by an effect on dispersion of sound before the reaction proper occurs.

Apart from this rule, light atoms like helium seem to favor dissipation of vibrational energy. Eucken explains this property of helium by its

small diameter, which allows it to penetrate more deeply into the structure of other molecules. Furthermore, Eucken and Jaacks (16) assume that collisions, the duration of which nearly coincides with the period of one vibration, are particularly effective in dissipating vibration.

One can not expect that considerations as simple as that can completely explain the interaction of atoms and molecules. For example, the great difference between the effects of hydrogen and deuterium on dispersion of sound in ethylene, observed by Richards (69), can hardly be explained so simply.

The rule of Eucken and Becker has been interpreted on the basis of potential surfaces as derived from wave mechanics by Eyring, Gershinowitz, and Sun (18), in connection with their theory of triple collisions (see sections III E and III G). In the same paper they explain the great efficiency of hydrogen by the fact that it can readily form a complex molecule with other substances, since it is in a favorable configuration about half the time at room temperature. This is due to its small moment of inertia.

Patat and Bartholomé (61) recently introduced the hypothesis that the high persistence of vibration in molecules when colliding with molecules of the same type is correlated with a high probability for the complete transfer of vibration from one molecule to another by resonance acting between equal particles. This will be further discussed in section III G.

Comparing results of dispersion of sound with spectroscopic results (section III B) from the point of view of the chemist, there is a preference for dispersion of sound. The reason is that in sound experiments no electronic excitation and no high vibrational quanta, but only the lowest vibration of the normal electronic level, play a part. This energy range, just exceeding the thermal average, is most important in chemical activation by heat. It is to be expected, therefore, that conclusions from dispersion of sound apply more directly to thermochemical processes than conclusions from most spectroscopic investigations as far as they deal with excited electronic levels.

It is striking that—apart from the wide range of probabilities—the order of magnitude of the number of collisions required for dissipation of the lowest vibrational quanta is in any case large as compared with unity. This number materially decreases with increasing temperature.

#### *D. Time lag of specific heats of gases in explosions*

In the measurement of specific heats of gases at high temperatures by the explosion method deviations are observed between experimental and theoretical values (12). Wohl and Magat (91) explain these effects on the basis of the idea—taken from the theory of dispersion of sound—that

the vibrations of  $N_2$  and  $O_2$  approach thermal equilibrium with a certain time lag. This idea in particular explains the fact that traces of water present reduce the time lag, that is, accelerate the exchange of vibrational energy in collisions. As the explosion method is subject to various sources of error, hardly any numerical results comparable to the results of dispersion of sound can be expected.

*E. Rate of recombination of atoms or radicals in triple collisions*

Another group of observations, very different in its technique but related in the elementary processes involved, is concerned with the recombination of atoms or radicals. We are not interested in the wall effect, but only in collisions between gaseous atoms and molecules. It is well known that two hydrogen atoms in the ordinary binary collision have scarcely any chance to form a molecule. The reason is that they fail to get rid of their energy of combination unless there is a third body present in the collision carrying away some of the energy and so catalyzing the combination. Since the pair of colliding atoms may well be described as a molecule with vibrational energy beyond the limit of dissociation, the effect of the third body is to reduce the energy of vibration of the hydrogen molecule in a collision.

The experimental work on this process, largely reviewed in the book of Kassel (38), although not agreeing well in detail, shows consistently that a third particle in a triple collision with two hydrogen atoms has the efficiency of the order of magnitude of unity in catalyzing the combination (1, 80). This means that in this limiting case the vibrational energy fails to show appreciable persistence.

Recently the recombination of halogen atoms has been investigated. Rabinowitsch and Wood (66) observed the change of concentration of bromine and iodine molecules caused by intense illumination with a sensitive optical method. Hilferding and Steiner (33) inferred the rate constant of the recombination by observing to what extent the formation of hydrogen bromide is affected by added gases. Again we are primarily concerned with the order of magnitude of the effect. It is in the neighborhood of unity for most added gases,—quite different from all collision effects observed by dispersion of sound. Rabinowitsch (65) concludes that the effect per collision increases with the size of the molecule acting as third body and the intensity of the field surrounding the molecule. The results do not quite agree with their numerical values.

Investigating the recombination of OH radicals and H atoms with the aid of absorption spectra of OH taken in snapshots, Frost and Oldenberg (24) showed that triple collisions are required. Again they have a rate constant of the order of magnitude of unity.

The observation in these cases of recombination is restricted to the fact that triple collisions lead to real molecules, that is, to values of vibration somewhere below the critical limit. It is of minor importance that the rotation might contain energy exceeding the energy of dissociation by a certain amount (57).

Must we assume that the largest part of the vibration is carried away in the triple collision so that almost non-vibrating molecules are produced? That this is probably not the case follows from a comparison with the results discussed in the preceding sections. Excited iodine molecules with high vibration have the tendency to give away some vibration in collisions but only a small amount each time (section III B). Another argument leading to the same result is as follows: chlorine shows no persistence of vibration near the convergence limit. (This is inferred by analogy with bromine and iodine actually investigated by Rabinowitsch and Wood.) On the other hand, chlorine shows a very high persistence of its lowest vibrational quantum in dispersion of sound. We infer that the pair of atoms, when forming a molecule in a triple collision, does not lose at once the largest part of its vibrational energy, since such a loss would reduce the vibration to the range in which it is much more persistent.

While the order of magnitude of unity has been found for the simple recombination processes observed, a certain factor may be predicted which may materially reduce this probability for more complicated radicals. Only those collisions are expected to result in recombination in which the configuration of the partners is approximately the same as in the molecule to be formed. A restriction like that has been postulated for various reactions in gases, in particular by Rice and Gershinowitz (68) and by Vaughan (86).

The theoretical understanding of the effect of triple collisions in catalyzing the recombination of atoms is based on the wave-mechanical treatment given by Eyring, Gershinowitz, and Sun (18) (see section III G). They succeed in calculating the absolute rate of recombination of  $H + H$  with another  $H$  acting as a third body in good agreement with experimental results. They estimate that  $H$  is at least six times more effective than  $H_2$  as a third body, in good agreement with the measurements of Amdur (1). Comparing the relative efficiencies of various gases as third bodies they are able to predict from their theory that the order should agree to the order of their reactivities with  $H_2$ . This rule is well supported by Bonhoeffer's (7) measurements. It is the same rule that Eucken and Becker had derived from experiments for dispersion of sound.

The obvious difference between recombination in triple collisions and the processes discussed in the preceding section is that in the dispersion of sound experiments we are dealing with quanta of vibration so large that

they are comparable to  $kT$ . Here, however, we are dealing with energies to be carried away that belong to a continuous range beyond the limit, or to a quantized range near to this limit which by its large number of small quanta might behave similarly to a continuous range.

#### *F. Activation of unimolecular decompositions*

Our interest in unimolecular decompositions, which have recently been reviewed by several authors (39, 49, 62) from a general point of view, is restricted to the special question: How do they manifest the probability of gaining vibration in collisions? Obviously this question is equivalent to the other, dealt with in the preceding sections: How large is the probability that a vibrating molecule gives away energy in collisions?

In a bimolecular decomposition a collision process directly causes dissociation. In complicated molecules it can happen instead that the collision process directly produces vibrations in several degrees of freedom. These are coupled so that they are able to exchange energy among each other. So for a given total energy content of a molecule, a certain probability results for a concentration of energy in one degree of freedom sufficient to decompose the molecule. As these probabilities are intrinsic in the molecule it decomposes without further collisions after a certain lifetime. If this lifetime is small as compared with the time between two collisions (low pressure), it does not become manifest and the reaction is bimolecular. *Vice versa*, if the activation is frequent above a certain limit (high pressure) and the following decomposition infrequent (long intrinsic lifetime of activated molecules), the number of activated molecules is practically determined by thermal equilibrium and becomes independent of the number of activating collisions. So the reaction becomes unimolecular. The critical pressure range at which the reaction changes from bimolecular to unimolecular indicates how frequent collisions are required to maintain a sufficient supply of highly vibrating molecules.

For a given molecule that shows unimolecular decomposition, Hinshelwood (34) and his collaborators found that the critical pressure strongly depends upon the type of gas added. This indicates that the various molecules have very different abilities to impart vibration by collisions to the molecule to be decomposed. Here is another experimental method contributing information of the kind considered in the preceding sections.

Examples of the yield per collision with which various added gases activate  $F_2O$  (47),  $N_2O$  (87, 89), and azomethane (78) are given in table 2.<sup>3</sup>

Again, as in dispersion of sound, light atoms seem to have a stronger effect than heavy atoms, as is best evident from the comparison of rare gases.

Investigating organic compounds, Hinshelwood and his coworkers found



that in most cases hydrogen is about as effective in causing activation as the organic molecule itself; many molecules are considerably less effective. This effect of hydrogen has been largely explained on the basis of wave-mechanics by O. K. Rice (cf. the report of Zener (95)) and by Eyring, Gershinowitz, and Sun (18).

While the relative probabilities given in table 2 are derived directly from experiments, the absolute values are much less certain. For pure nitrous oxide the probability 1/1700 results when all four vibrational degrees of freedom are supposed to be involved. With three degrees of freedom the result (88) is 1/190 and with two it is 1/12. Patat and Bartholomé (61), on the basis of a more indirect estimate, applying results of dispersion of sound, obtained the order of magnitude of unity.

TABLE 2

*Relative yields per collision of gases activating unimolecular decomposition*

DECOMPOSITION OF $\text{F}_2\text{O}$ (AT 250°C.)		DECOMPOSITION OF $\text{N}_2\text{O}$ (AT 653°C.)		DECOMPOSITION OF AZOMETHANE (AT 310°C.)	
Added gas	Yield	Added gas	Yield	Added gas	Yield
$\text{F}_2\text{O}$	1	$\text{N}_2\text{O}$	1	Azomethane	1
$\text{O}_2$	1 13	$\text{H}_2\text{O}$	1.50	$\text{H}_2\text{O}$	0 46
$\text{N}_2$	1 01	$\text{CO}_2$	1.32	$\text{CO}_2$	0 25
$\text{F}_2$	1.13	$\text{N}_2$	0.24	$\text{N}_2$	0 21
$\text{SiF}_4$	0.88	$\text{O}_2$	0 23	$\text{CH}_4$	0.20
He	0.40	He	0.66	CO	0 13
A	0 52	Ne	0 47	$\text{D}_2$	0 37
		A	0 20	He	0 07
		Kr	0.18		
		X	0.16		

In the preceding sections we differentiated the evidence dealing with the lowest quantum of vibration (dispersion of sound) and with high quanta near the limit (recombination of atoms, fluorescence radiation). The activation of unimolecular decompositions holds an intermediate position. While most degrees of freedom of the decomposing molecule certainly contain only a small fraction of their maximum energy content, the decomposition indicates that there is one degree of freedom that reaches its limit by the activation process.

### G. General rules

1. *Purpose of general rules.* The experimental results reported in the preceding sections suggest general rules. The experiments, however, do not cover the ground so completely that at the present time the final shape of such rules can be given. Yet an attempt like this might be well worth

while for two purposes—first, in order to find deficiencies in the experimental evidence and, secondly, in order to apply such rules to theories of gas reactions in which they have been rather neglected.

2. *Translation.* There is no doubt, theoretical or experimental, that translation is well described by classical physics. Rapid dissipation by elastic collisions is certain. Translation, therefore, has a chance to act as energy of activation only if the atom or radical produced with high energy has a chance to react without many intervening collisions. The ratio of masses, however, of the various partners must be considered. This is illustrated by the extreme case of free electrons keeping their high temperature separate from the temperature of the gas.

Apart from the collisions intervening between activation and reaction, at the reaction proper energy of translation can only partly be spent because of the classical laws of conservation. This was illustrated in section III A by the example of the collision  $\text{Cl} + \text{H}_2$ .

3. *Vibration.* Dissipation of vibration is observed as a rapid process in fluorescence radiation of iodine when modified by pressure, and in triple collisions leading to the combination of free atoms. In both cases we are dealing with very small quanta of vibration. In the excited iodine molecule, their energy is 0.01 volt-electron, and in the combination process we are even dealing with the limiting case,—vibrational quanta approaching the smallest values near the limit of dissociation. We infer that in cases in which the vibrational quantum is smaller than  $kT$ , the collision process is described with reasonable approximation by classical mechanics.

On the other hand a most pronounced persistence has been observed in dispersion of sound. In this case we are dealing with the lowest, that is largest, vibrational quantum which fails to be dissipated into heat in many thousand collisions with equal molecules or molecules of some other kind, specific in each case. Because this quantum is not small as compared to  $kT$ , classical physics fails to describe the collision process. The rules for dispersion of sound are given by Eucken and Becker: Light particles show a certain preference to dissipate energy. Still more striking is the other rule that partners with a chemical affinity for the vibrating molecule show a strong power to dissipate energy, although actually under the conditions of the sound experiment no reaction takes place.

The correlation between the persistence and the size of the quantum, suggested by the experimental results, does not agree with the recent argument of Patat and Bartholomé (61) and of Eucken (14). They assume that the persistence is independent of the number of vibrational quanta excited. They support this assumption by recent theoretical results of Landau and Teller (50). But since these results are derived for the harmonic vibrator, the theory fails to describe the change of persist-

ence due to the decreasing size of the quanta with increasing quantum number. On the other hand, such a change is experimentally observed for hydrogen and chlorine. In both gases the lowest quanta are persistent (spectroscopic observation for hydrogen; dispersion of sound for chlorine); nevertheless in both gases the highest quanta are readily dissipated (recombination of atoms in triple collisions). This comparison within the same gases proves that persistence is characteristic only for the lowest, that is, largest quanta.

The temperature effect on persistence of vibration is consistent with our point of view: With increasing temperature, that is increasing  $kT$ , the persistence of vibration in collisions becomes less pronounced. This temperature effect on the persistence, however, is equally well described by Patat and Bartholomé on the basis of the idea that the closer the approach at the collision, the stronger ought to be the interaction, hence the higher the probability of an exchange of energy.

4. *Rotation.* In dispersion of sound no trace of persistence of rotational energy in collisions can be detected. Correspondingly in fluorescence radiation of iodine vapor an easy transfer of rotational energy is observed. Some persistence, however, has been detected by other spectroscopic methods which are presumably more sensitive than sound experiments, as the time interval during which persistence is observed is given by the lifetime of an excited electronic state instead of a period of sound. Persistence of rotation is evident in the electric discharge through hydrogen.

The comparative lack of persistence of rotation is presumably connected with the fact that rotational quanta are much smaller than low vibrational quanta. In the exceptional cases in which some minor amount of persistence is evident, the rotational quanta are larger than in most other molecules. In particular in N. D. Smith's (81, 82) investigation of the effect of temperature, the persistence of rotation of hydrogen molecules becomes more striking when at liquid air temperature the quantized rotational energy to be dissipated becomes comparable to or larger than  $kT$ . In hydrogen no less than two rotational quanta can be given away because of the well-known properties of the nuclear spin in homonuclear molecules (54, 95). These energy steps of the excited hydrogen molecule,  $E_{j+1} - E_j$ , in volt-electrons are given in table 3. At liquid air temperature the value of  $kT = 0.0077$  volt-electron is smaller than the energy steps; at room temperature  $kT = 0.025$  is of the same order.

5. *General rule.* The experiments discussed suggest a rule which *a priori* seems plausible: No pronounced persistence or vibration or rotation in collisions occurs if the quanta are much smaller than  $kT$ ; if the opposite holds, persistence might take place, but it is a specific property of the partners in the collision. This difference in the persistence of quanta of

different sizes, derived from experimental evidence, agrees well with Zener's theoretical rule (95) that internal energy will be dissipated much more rapidly if it can be given up to energy of translation as several small quanta than as one large quantum.

Comparing the specific effects among various partners by dispersion of sound, Eucken and Becker found the general rule which correlates the persistence—ranging from 47,000 down to 40 collisions—with the chemical reactivity of the partners.

6. *Quantum theory of the energy transfer in collisions.* Simple cases of energy transfer in collisions have been treated by quantum mechanics by applying the perturbation theory to the Schrodinger equation for the system. Zener (95) has recently reviewed this work and, also, has contributed a great share to it (see the following section on "resonance"). To what extent the results have been affected by the far-reaching simplifications, indispensable for the mathematical treatment, is difficult to estimate.

TABLE 3  
*Rotational energy differences of excited H<sub>2</sub> (in volt-electrons)*

<i>j</i>	0	1	2	3	4	5
$E_{j+2} - E_j$	0.02	0.037	0.053	0.066	0.080	0.092

Great progress is due to the representation of simple collision processes by potential surfaces introduced by Eyring and Polanyi (19). The collision process  $H + H_2$ , which has been discussed in great detail, encounters the lowest potential wall, when all three atoms move along a straight line. For this case the potential energy as a function of  $r_1$  and  $r_2$  (mutual distances between adjoining atoms) is represented by a surface,—conveniently drawn as a contour map. The two possible molecular states are represented by valleys and the complete separation of all three atoms by a high plateau for large  $r_1$  and  $r_2$ . For a special angle between the coordinates (depending on the mass ratio) the surface has the property that the mechanical motion of a masspoint, traveling over the surface, describes a curve, which by its coordinates,  $r_1$  and  $r_2$ , represents a possible motion of the three particles. Hence the probability of formation of a molecule by a triple collision can be computed as the probability that a masspoint, approaching the valleys at random, will finally roll into one of the valleys.

These contour maps give admirable pictures of the motion. From such a map designed for  $H + H + H$ , Eyring, Gershinowitz, and Sun (18) derived their conclusions discussed in sections III C and III E. Dr. Gersh-

inowitz kindly informed us of his extension of this theory (26), in which he applies the same method to a rare gas atom colliding either with a pair ready to form a molecule (triple collision) or with a molecule with little vibration (as observed in dispersion of sound). In both cases he compares the effect of helium as a third body with the effect of H. The potential surfaces of  $\text{He} + \text{H} + \text{H}$  are very similar to those of  $\text{H} + \text{H} + \text{H}$  as far as the bottom of the valleys are concerned, but they differ considerably at the rims. He concludes that the molecule with little vibration, represented by the bottom, is affected by helium in approximately the same way as by some other particles. The corresponding observation is that in dispersion of sound helium has about the same effect as many other particles. On the other hand near the rim of the valley (pair of colliding atoms) the specific properties of the potential wall provided by the helium atom account for the relative inefficiency of helium in triple collisions or unimolecular reactions. In general the relative efficiency of energy transfer is not only a specific property of the molecules involved, but is also dependent upon the degree of excitation of the system. There is no *a priori* reason why the relative efficiencies of gases in transferring energy should be the same for dispersion of sound and reaction rates. They might be different again in heat conductivity or in viscosity which is largely determined by the external degrees of freedom, translation, and rotation.

7. *Relation to "resonance."* Is there any rule for collisions in which vibration or rotation is given away indicating the degrees of freedom into which the energy probably changes? Since vibration and rotation are quantized we might expect "resonance," that is, nearly complete transfer in a collision of quantized energy due to the more or less accurate coincidence of energy levels. Resonance is known to be the most important factor in "collisions of the second kind" in which electronic energy is exchanged between atoms. There is a definite tendency observed that electronic energy remains concentrated as electronic energy in the transfer so that the smallest possible amount of energy goes into translation (83). On the other hand, if we apply classical physics, we expect that, for example, vibration far exceeding the thermal average should show a tendency to spread over all degrees of freedom available at the collision,—degrees of freedom of the partner and the vibrating molecule itself.

In our search for some direct evidence of resonance in the transfer of rotation or vibration we failed. One might search for such a case in investigations of band spectra as modified by added diatomic gases. No evidence of it could be found in the literature. More experimental work seems desirable.

There are a few cases which indicate that energy of vibration given away is distributed over several degrees of freedom. In the electric dis-

charge through hydrogen with helium the disappearance of high vibration can be observed together with a simultaneous increase of rotation, the rotation, however, gaining only a part of the energy of vibration lost; obviously the balance goes into translation. Similar is the process observed in the fluorescence radiation of HgH. In these cases the tendency of dissipation over the degrees of freedom available seems to prevail.

It is to be expected—on the basis of “resonance” as well as on the basis of classical mechanics—that a degree of freedom which before the collision has a large amount of excess energy does not gain any more by collisions. This is observed in the fluorescence radiation from  $I_2$ . Actually, collisions during the lifetime of the excited state take away vibration but never contribute additional vibration.

The failure to find direct evidence of resonance in the transfer of rotation or vibration—inadequate as the experimental evidence is—is well understood in cases in which from mechanics the production of a considerable amount of translation is to be expected. This is most evident in the transfer of rotation into rotation since such a transfer can hardly take place without the centers of gravity of the molecules picking up kinetic energy (58). (An exception would be the limiting case, represented, for example, by HgH, in which the kinetic energy of rotation because of the mass ratio is centered in the hydrogen atoms. According to the laws of impact, transfer of rotation energy may happen with a negligible amount of translation being produced.) A similar mechanical objection holds against resonance, that is *complete* transfer, in the exchange between rotation and vibration. It would violate the law of conservation of angular momentum.

The case is not clear, however, in the transfer of vibration into vibration. It is true that the simple picture of this transfer, consisting in a mechanical knock of vibrating particles, would necessarily lead to some energy being imparted to the centers of gravity so that the translation would spoil the resonance.

However, resonance would not be excluded by the principles of mechanics if, instead, we describe the transfer of vibration into vibration by the picture of Eucken and Franck (section III C): during the collision process, one molecule by its close approach modifies the field of force acting within the other molecule and so starts vibration.

While no case of resonance other than electronic was known in the transfer of energy of heavy particles in collisions, a high probability, even of the order of magnitude of unity, caused by resonance has recently been assumed by Patat and Bartholomé (61) on the basis of the following, rather complicated argument. They compare dispersion of sound, activation of unimolecular reactions, and recombination by triple collisions. Within each group they compare the effects in pure gases with those in

mixed gases, that is, the efficiency of equal and foreign molecules in dissipating excess energy. They conclude from the experimental evidence that equal molecules prove very effective in unimolecular reactions and triple collisions, but very ineffective in dispersion of sound. In order to describe these facts they assume as a general principle that equal molecules are very effective in the transfer of vibration into vibration by resonance. By this idea they explain the dissipation of energy by collisions in unimolecular reactions and triple collisions. In dispersion of sound, however, the situation is peculiar in that only the one lowest vibrational quantum comes into play. The authors assume a very frequent transfer by resonance. But this peculiar case of resonance does not become manifest, since the transfer of the lowest quantum from one molecule to another has no effect on the observations. So they correlate the ineffectiveness of molecules of the same gas with a transfer, not at all excluded, but instead taking place with a probability of the order of magnitude of unity. This would lead, for example, in carbon dioxide (see table 1, section III C) to a transfer of vibration in collisions taking place with the order of magnitude 47,000 times before dissipation.

Objections are as follows: (1) Resonance can hardly increase the effectiveness of triple collisions like  $\text{Br} + \text{Br} + \text{Br}_2$ . The reason is that the pair  $\text{Br} + \text{Br}$  is ready to give away its highest vibrational quanta while  $\text{Br}_2$  is ready to receive its lowest vibrational quanta. The size of these quanta differ so that, on the basis of resonance,  $\text{Br}_2$  is not expected to have a greater effectiveness than other molecules. (2) In dispersion of sound equal molecules are not greatly distinguished from some foreign molecules. This is evident from table 1 (section III C). (3) Both for unimolecular reactions and triple collisions<sup>4</sup> the experiments (see table 2, section III F) do not indicate a pronounced preference for the effect of equal molecules. In both of these cases one might rather infer from the experiments a preferred effect of diatomic and polyatomic gases as compared with monatomic gases. Patat and Bartholomé explain such a preferred effect of molecules by their ability to take up energy in more degrees of freedom than the monatomic gases.

It can hardly be said that in dispersion of sound the hypothesis of a frequent transfer of vibration from one molecule to another explains the unexpected fact that this energy withstands dissipation. Since the vibration is not destroyed but only transferred, it remains available for dissipating collisions. (The argument is different for excited, highly vibrating iodine molecules (section III B) which in collisions have a great chance to lose electronic energy. This destroys all future possibility to observe what happens to their vibration.) It seems evident that in collisions between polyatomic molecules like carbon dioxide a transfer of vibration by resonance can take place only for a rather special configuration of the two colliding molecules. Hence many collisions must happen without such transfer of vibration. Their failure to dissipate the vibrational energy remains unexplained.

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<sup>4</sup> The table of probabilities of triple collisions given by Patat and Bartholomé is not reproduced since, according to Rabinowitsch, some results are questionable.

The experimental proof for a very high probability of the transfer of vibration into vibration seems to us not conclusive. It may be assumed that such a probability, as far as it exists, is largest among equal molecules because of resonance. The objection holds only against the high absolute value of this probability as inferred from experiments.

The theoretical treatment given by Zener (95) leads to such an effect of resonance on the probability of transfer. But the numerical value of this probability is very small when compared to unity; for example, in collisions between two nitrogen molecules, one of them vibrating, the theoretical probability of transfer is only of the order of magnitude  $10^{-5}$ . Zener's theory, however, does not deal with exactly the same processes as the hypothesis of Patat and Bartholomé. Zener only estimates the probability of a transfer of vibration into vibration, in particular for equal molecules. He is not concerned with competing transfers of vibration into other degrees of freedom, whereas Patat and Bartholomé—deriving their hypothesis from experimental results of the lifetime of vibration—deal with all possible types of transfer.

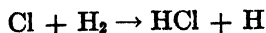
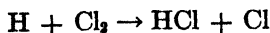
It seems to be a rule that resonance which dominates the transfer of electronic energy has no great effect on the exchange of the quantized energies—vibration and rotation—between heavy particles. Instead dissipation of energy among all degrees of freedom available seems to prevail. The transfer of vibration into vibration represents a possible exception to this rule which it is hoped will be cleared up by more experimental work.

#### IV. APPLICATION TO GAS REACTIONS: ENERGY CHAIN REACTIONS

The general rules derived in the preceding sections have application to all types of gas reactions. In particular, two types of gas reactions have already been discussed because of the information which they give us concerning the transfer of energy in collisions. We shall now discuss the application to energy chain reactions.

##### *A. General characteristics of energy chain reactions*

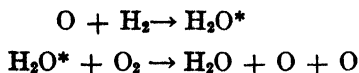
Chain reactions may be classified theoretically into two types: first, atom or radical chain reactions, such as in the hydrogen-chlorine reaction



where the atoms H and Cl are the "chain carriers," or second, energy chain reactions in which one or more chain carriers are considered to be



ordinary molecules with excess internal energy. For example, a suggested mechanism of the hydrogen-oxygen reaction is



the asterisk indicating an "activated molecule,"—a molecule with excess energy. Here the excess energy of the first step of the reaction is assumed to be transferred specifically to the oxygen molecule. Atom or radical chain reactions will not be discussed here, because these reactions are merely a set of successive ordinary chemical processes. Energy chain reactions, however, are of a more physical nature since they depend upon the persistence of internal energy.

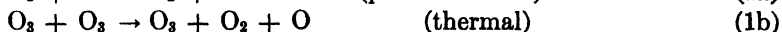
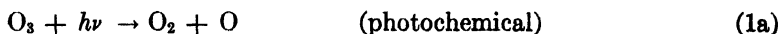
The concept of energy chain reactions was first introduced by Bodenstein (6) to explain the photochemical combination of hydrogen and chlorine,—a reaction which is now explained by the atom chain used above as an example. Later Christiansen and Kramers (8) applied the idea of energy chains to explain the unusually high speed of certain unimolecular reactions. This application was also replaced by a preferable theory. No doubt these early unsuccessful attempts to use the idea of energy chains contributed to the present tendency of always giving preference to an atom or radical chain mechanism over an energy chain mechanism.

In order for an energy chain to be possible the activated molecule which acts as a chain carrier must have a lifetime at least as great as the time between collisions with a reactant molecule, i.e., it must have a good chance of not being deactivated before it completes its link in the chain. Clearly then we have here an excellent opportunity to make use of the conclusions of section III to determine the reasonableness of certain postulated energy chains. Only activated molecules with particular types of electronic or vibrational energy can conceivably persist through many collisions without deactivation. In particular, metastable electronic states have a sufficient lifetime to take part in an energy chain. Furthermore, they transfer their energy specifically to molecules with which there is resonance (36, 37, 90). These two characteristics cause molecules in metastable electronic states to behave as though they were different chemical species from the same molecules in their normal states. In section III it is concluded that persistence of vibration might occur if the energy difference between vibrational energy levels is comparable to or greater than the mean thermal energy  $kT$ . In this case there is some specificity in the transfer of the energy to other molecules, but certainly there is no such well-defined resonance effect as exists in the transfer of electronic energy.

The conclusion that may be drawn from this discussion is that energy chain reactions can most probably occur if the chain carriers are in metastable electronic states. Chain reactions involving activated molecules in high vibrational states are not so probable. With this in mind we now consider two postulated examples of energy chains.

### *B. Decomposition of ozone*

After many years of experimental study of the thermal and photochemical decomposition of ozone there is at present some agreement as to the mechanism of the reaction. (For a brief review consult Semenov's book (77), p. 400.) The steps in the reaction are believed to be as follows:



It is apparent that steps 2 and 3 constitute an energy chain. The chain length of course depends on the ability of steps 4 and 5 to break the chains. According to Heidt and Forbes (30), the photochemical quantum yield—molecules of ozone decomposed per quantum of light absorbed—which is a lower limit to the chain length varies from less than one to more than six. If step 3 were unimportant the quantum yield could be no greater than two. The fact that it can be greater than two requires assuming a chain reaction. Since no atom or radical chain mechanism can be devised, it is necessarily an energy chain.

Reaction 5a is about three times more probable than reaction 3, or the chances are about three to one in favor of a deactivation of the chain carrier before it can react. The efficiency of foreign molecules in causing deactivation (reaction 5b) has been investigated by Beretta and Schumacher (2). They find that oxygen, carbon dioxide, and nitrogen are slightly less effective than ozone and that the inert gases are less effective by at least an order of magnitude. The absolute rates of these processes cannot be determined from the experimental data, so that it is not known whether there is persistence of the activated molecule through many collisions with ozone or other molecules. However, persistence is not necessary to explain the reaction.

These data do not enable one to decide whether the  $\text{O}_2^*$  is in a high vibrational state or in a metastable electronic state. Energy considerations are of interest in this connection. Reaction 2 is exothermic by 83

kg-cal., so that each oxygen molecule resulting may have at least 41 kg-cal. of activation. The dissociation of ozone into  $O_2$  and  $O$  requires only 24 kg-cal., so that there is plenty of energy available for reaction 3. It is known spectroscopically that  $O_2$  has a metastable  ${}^1\Sigma$  electronic state with an energy of 37 kg-cal. Heidt (29) suggests that the chain carrier is this metastable state,—an assumption which is probably preferable to assuming that it is a high vibrational state.

In spite of the uncertainties the decomposition of ozone probably provides the best example of an energy chain reaction.

### C. Low pressure explosion of hydrogen and oxygen

As another example of a possible energy chain we now consider the interesting low pressure explosion of hydrogen and oxygen. This is one of a group of low pressure explosive oxidation reactions and so is of general interest. The reaction has been reviewed by Hinshelwood and Williamson (41) and by Semenov (77). Most work has had to do with the attempt to determine the mechanism of the reaction not by studying the rate of the reaction in the usual way but by studying the explosion limits. At a given temperature between approximately 450° and 550°C. there are two limiting values of the total pressure of a given hydrogen-oxygen mixture between which explosion can occur. The explosion limits of course depend on the temperature and composition of the gas mixture.

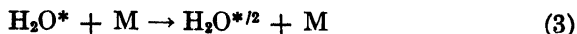
The general characteristics of the reaction are adequately explained by the theory of *branching* chain reactions. The exact mechanism of the branching chain, however, is unknown. No atom or radical chain has stood the test of experiment, so an energy chain is in order. Semenov (77) has tentatively suggested the following:



As no suitable *electronic* level of  $H_2O$  is known it is assumed that  $H_2O$  is in high *vibrational* level. Its total energy supplied by the formation process (1) is 115,760 kg-cal. In the transfer process (2) 117,300 kg-cal. are required. Hence reaction 2 involves the assumption that  $H_2O^*$  does not suffer any loss by intervening collisions. Furthermore, since the vibrational energy of  $H_2O^*$  is probably distributed over several degrees of freedom, reaction 2 involves a concentrated transfer of all this energy into one degree of freedom of a colliding molecule. According to the discussion given in section III, these assumptions are highly improbable. The difficulty becomes still greater by the following consideration. The experimental data for the upper explosion limit indicate that the chain branching

process—that is, reaction 2—has an activation energy of 24 to 26 kg-cal.; the colliding molecules must have this amount of thermal energy in addition to any special energy which the chain carriers may supply. But an activated molecule such as  $\text{H}_2\text{O}^*$  could certainly not persist through  $10^6$  to  $10^7$  collisions which this activation energy requires.

In order to improve the mechanism Semenov (76) has recently suggested the following additional processes in which deactivation is allowed but counteracted by a possible return of a partially deactivated molecule to the activated state:



$\text{H}_2\text{O}^{*/2}$  indicates a molecule that has lost approximately one half of its original energy of formation. Undoubtedly process 3 is quite probable. But reaction 4 followed by reaction 2 means that energy which has already been dissipated over several degrees of freedom becomes concentrated again—in spite of intervening collisions—first in the various vibrations of one water molecule, next still more concentrated in the one vibration of oxygen. This is against all experimental evidence (section III G) indicating a tendency towards gradual dissipation of excess energy over all degrees of freedom available. Although it is probably necessary to use an energy chain, this particular mechanism does not agree with the various results discussed above.

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## HYDROCARBONS FROM CARBIDES

GARTH L. PUTNAM AND KENNETH A. KOBE

*Department of Chemistry and Chemical Engineering, University of Washington,  
Seattle, Washington*

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The past few years have witnessed the development of an enormous chemical industry based upon the hydrolysis of calcium carbide (74). Acetylene resulting from this reaction may be easily hydrated to acetaldehyde, which, in turn, can be oxidized to acetic acid or reduced to ethyl alcohol. A single Canadian plant using this process has an annual capacity of 50,000 tons of glacial acetic acid (6). Plastics (4), solvents, even a chemically resistant product with physical properties similar to those of rubber are successfully manufactured (6). Table 1 gives some idea of the magnitude of the domestic carbide chemicals industry (1, 67).

The development of a synthetic organic chemicals industry based on the carbide of calcium lends interest to a study of some of the other carbides, several of which yield pure acetylene or its reduction products, while others give such diverse hydrocarbons as allylene, methane, and decane. Indeed, the fact that solid and liquid hydrocarbons result from the action of water on meteorites has in the past led many geologists to believe that petroleum was formed by the action of water on the core of the earth (7, 46). Although this theory of petroleum formation is no longer generally accepted, it is very likely that the first organic compounds of primitive times had their origin in this manner (31).

### CLASSIFICATION OF THE CARBIDES

The carbides may be divided into two main classes: (1) those which readily react with water or dilute acids, and (2) those which do not. Generally speaking, the carbides of the metals and metalloids whose oxides are acidic are not decomposable to hydrocarbons. In this class belong the carbides of boron (34), phosphorus (32), arsenic (32), vanadium (42), tungsten (34), tantalum (34), chromium (34), molybdenum (34), silicon (34), titanium (55), and zirconium (34). The carbides of metals whose oxides are basic are readily hydrolyzed: thus, the carbides of sodium, calcium, cerium, magnesium, and aluminum readily react with water, while the carbides of copper, silver, iron, and manganese react with



dilute acids (34). On the basis of chemical and crystallographic structure, the carbides decomposable by water or mineral acids may be further subdivided into three groups (52).

*Group I.* The crystal lattice is such that the carbon atoms are separated from each other by metal atoms. This group comprises the carbides of nickel, iron, cobalt, and manganese having the formula  $M_3C$ , and the carbides of beryllium and aluminum,  $Be_2C$  and  $Al_4C_3$ , respectively. The products formed on treatment with water or dilute acids result from the action of nascent hydrogen on each separate carbon atom. Methylene ( $CH_2=$ ) radicals are the primary product, and these, by hydrogenation and/or polymerization, are converted to methane and other hydrocarbons. Acetylene is not formed by the decomposition of these carbides.

TABLE 1  
*Carbide chemicals manufactured in the United States\**

CARBIDE CHEMICALS	1933	1931	1929	1927
Calcium carbide:				
Tons . . . . .	101,488	128,263		201,955
Value . . . . .	\$6,059,205	\$8,024,029		\$9,397,556
Acetylene:				
Thousands of cu. ft. . . . .	734,089	742,898	969,534	682,481
Value . . . . .	\$11,038,959	\$12,911,727	\$16,553,763	\$16,196,388
Glacial acetic acid:†				
Lbs. . . . .	36,359,413			
Value . . . . .	\$2,223,965			

\* Includes only chemicals manufactured for sale as such.

† By far the greater part, but not all, of the glacial acetic acid was manufactured by the calcium carbide process.

Two representative examples of group I are illustrated in figure 1. X-ray analysis of the iron carbide crystal has shown that each carbon atom is completely enclosed by an octahedron of iron atoms. Since each carbon atom is so completely surrounded by iron atoms, there is ample opportunity for reduction of the carbon by nascent hydrogen. Similarly, in the beryllium carbide crystal each carbon atom is enclosed by a cube of beryllium atoms. It is therefore not surprising that pure methane is formed by the hydrolysis of beryllium carbide. (However, as we shall see later, the high polarization potential of the evolved hydrogen may also favor the formation of methane.)

*Group II.* Carbides which give acetylene on hydrolysis comprise this group. The formation of acetylene is believed to be due to actual  $C\equiv C$  linkages in the crystal lattices of these carbides. Included in this group

are the carbides of the alkali, alkaline earth, and rare earth metals. Figure 2 illustrates a well-known member of Group II, tetragonal calcium

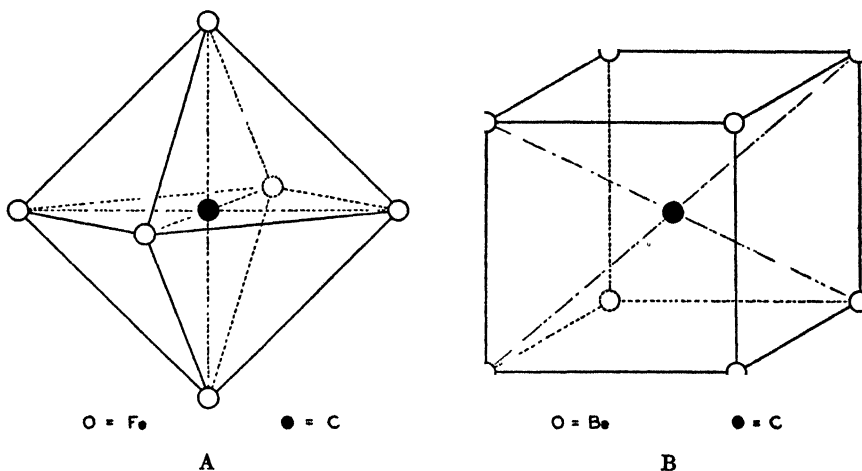


FIG. 1A. Relation of carbon to iron in iron carbide ( $\text{Fe}_3\text{C}$ ) crystal (34)

FIG. 1B. Relation of carbon to beryllium in beryllium carbide ( $\text{Be}_3\text{C}$ ) crystal (58)

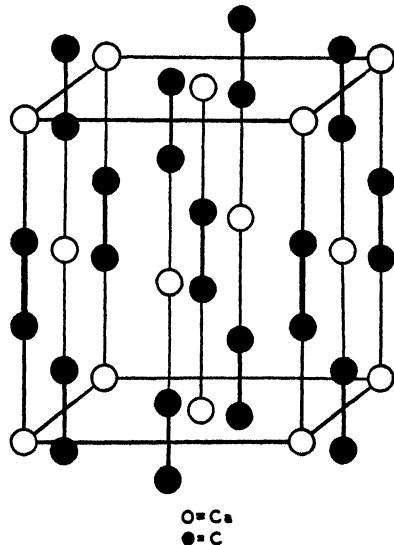


FIG. 2. Model of calcium carbide crystal

carbide. Six calcium atoms define the unit cell, a prism whose length is 6.37 A.U., and whose cross section (100 plane) is a square of edge 5.48 A.U. The carbon atoms are joined together in groups of two, forming

ions whose length is 4.2 A.U. and whose diameter is 3.3 A.U. When the carbide is hydrolyzed, this acetylenic linkage is preserved intact (57).

Thorium and the carbides of the rare earth metals give not only acetylene but also other unsaturated and saturated hydrocarbons. The irregular behavior of these carbides may be attributed to the conversion of the metal, upon decomposition of the carbide, from the bivalent to the trivalent or quadrivalent form, resulting in the formation of more hydrogen than that required for acetylene. That acetylene may be reduced in aqueous solution by nascent hydrogen has been shown by Traube and Passarge (60).

*Group III.* Carbides which yield allylene ( $\text{CH}_2\text{C}\equiv\text{CH}$ ) on hydrolysis comprise this group, of which magnesium carbide is the only known member. Although its crystal structure is not known, its hydrolysis to

TABLE 2  
*Hydrolysis of cementite to free carbon*

Molar concentration of sulfuric acid .....	2.5	2.5	2.5	0.017	0 017	0 017
Molar concentration of ferrous sulfate ..	0 0	0.60	1 39	0.0	0 60	0 96
Per cent of total carbon liberated.....	15	36	73	18	55	73
Molar concentration of benzenesulfonic acid.....	1.5	1.5	1 5	0.25	0.25	0.25
Molar concentration of ferrous benzenesulfonate.....	0.0	0 18	0.63	0.0	0.18	0.63
Per cent of total carbon liberated.....	33	60	97	34	60	87
Molar concentration of acetic acid .....	1.5	1.5	0.5	0.5		
Molar concentration of ferrous acetate....	0.0	0.385	0.0	0 385		
Per cent of total carbon liberated.....	41	70	68	99		

pure allylene would indicate the presence of  $\text{C}-\text{C}\equiv\text{C}$  linkages in the lattice.

#### EFFECTS OF CONDITIONS OF HYDROLYSIS ON PRODUCTS OBTAINED

Free carbon is invariably one of the hydrolysis products of pure cementite,  $\text{Fe}_3\text{C}$  (50). The data given in table 2 have been calculated from the results of Schenck and Stenkhoff (50), and were obtained by dissolving 0.200-g. samples of pure cementite in 600 ml. of solutions containing varying concentrations of acids and their corresponding ferrous salts. In each experiment the temperature was held constant at 60°C. The percentage of the combined carbon which was liberated by the action of each dissolving solution is given in table 2.

The results in table 2 show rather conclusively that the amount of carbon liberated as free carbon increases with both the pH and the ferrous-ion concentration. It has been suggested (50) that the increase in pH lowers the reaction rate, and consequently decreases the polarization or "overvoltage" (27) of the hydrogen on the carbide. This would cause the hydrogen to be less effective as a reducing agent, and more free carbon would be obtained. Similarly, increase in the ferrous-iron concentration would lessen the tendency of iron to go into solution, resulting also in a decrease in polarization. Nevertheless, an exact correlation between reaction rate and completeness of reduction is still lacking. For example, Moissan (36) found that when manganese carbide ( $Mn_3C$ ) was hydrolyzed, the use of hydrochloric acid in place of water favored the formation of hydrocarbons of lower hydrogen-to-carbon ratio, and Schmidt and Oswald (53), in more recent experiments with nickel carbide,  $Ni_3C$ , were unable to obtain reproducible results.

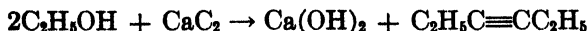
The temperature of reaction exerts an influence on the hydrolysis of cerium carbide, a greater proportion of the acetylene being reduced to ethylene and methane at room temperature than at  $0^\circ C$ . (36). Temperature also has a marked effect on the hydrolysis of calcium carbide. By passing steam at atmospheric pressure and  $500^\circ$  to  $700^\circ C$ . over calcium carbide, Plauson and Tischenko (43) were able to obtain up to 60 per cent yields of benzene. At the same temperature, but under reduced pressure, a mixture of aluminum and calcium carbides yielded pentinene, whereas polymerized products such as terpenes were obtained at higher pressures (43). Although neither of the pure carbides gives ethylene, the hydrolysis of a mixture of aluminum and calcium carbides at room temperature yields a small amount of the gas (47).

Apparently, contact agents may exert an influence on the hydrolysis products of carbides. Lebeau and Damiens (29) found that the presence of graphite in uranium carbide,  $UC_2$ , caused the hydrolysis to proceed more slowly. The evolved gases contained less hydrogen and more hydrocarbons than that produced from carbides containing no graphite (29).

Other peculiar examples are the manganese carbides ( $Mn_3C$  and  $Mn_5C_2$ ), which are formed by passage of excess of methane over manganese oxides at  $800^\circ$  to  $1000^\circ C$ . In this synthesis, the formation of carbides decomposable by water is favored by the presence of barium oxide and aluminum oxide. The formation of carbides whose hydrolysis requires a strong mineral acid is favored by nickelous oxide, chromic oxide, and ferric oxide. Compounds that exert little or no influence are potassium carbonate, calcium oxide, titanium dioxide, cupric oxide, vanadium trioxide, and cerium dioxide (15).

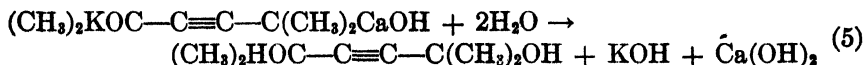
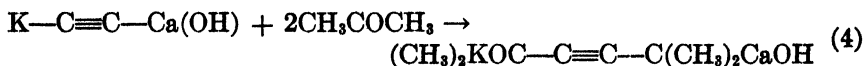
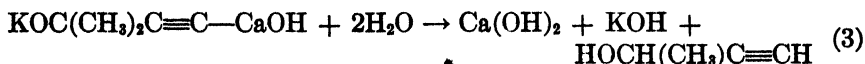
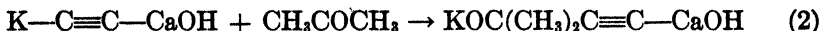
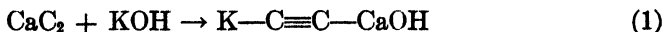
## DECOMPOSITION OF CARBIDES WITH ORGANIC COMPOUNDS

At 150° to 300°C., and under 12 to 40 atmospheres pressure, calcium carbide readily reacts with alcohols, phenols, or halogen derivatives of hydrocarbons, to form acetylenic compounds (9). Two examples of this type of reaction are:



Methyl alcohol, propyl alcohol, phenol, and many other compounds may be used as starting materials. When alcohol is used, part of the calcium carbide reacts to form calcium ethoxide and acetylene (36). Corson, who investigated this process, did not state the yields (9).

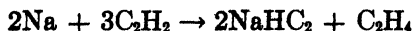
Calcium carbide also reacts with ketones, acetylenic alcohols being formed (26). For example, 3-methyl-3-hydroxy-1-butene may be obtained in 70 per cent yield by reacting acetone at a temperature of 0°C. with calcium carbide and potassium hydroxide in ether solution. When the reaction is carried out at a slightly higher temperature, a 74 per cent yield of 2,5-dimethyl-2,5-dihydroxy-3-hexene results. The probable reactions given by Kazarian (26) are as follows:



## CHEMISTRY OF THE METALLIC CARBIDES

*Alkali metal carbides*

Acetylene possesses marked acid properties, one hydrogen atom being replaceable under ordinary conditions (10, 35, 68). In the presence of an inert solvent, the alkali metals readily react to give the corresponding monobasic acetylide. Moissan first prepared the compounds  $\text{NaHC}_2$ ,  $\text{KHC}_2$ , and  $2\text{LiHC}_2 \cdot 3\text{NH}_3$  by passing acetylene into a solution of the alkali metal in liquid ammonia (35), a typical reaction being



No hydrogen is evolved, but a small amount of the acetylene is reduced to ethane (10). Similar results are obtained when boiling xylene is used as the solvent (13). Contrary to many statements in the literature (8), a liquid ammonia solution of  $\text{NaHC}_2$  will not react further with sodium (56, 68). The alkali metal acetylides are soluble in liquid ammonia, and the solutions are good electrolytic conductors (56).

On heating sodium acetylide to  $180^\circ\text{C}$ ., acetylene is evolved, and a white powder of *sodium carbide*,  $\text{Na}_2\text{C}_2$ , remains (35, 68). When prepared in this way, nitrogen compounds are always present in varying quantities (68), owing, presumably, to ammonolysis (10, 56). Sodium carbide decomposes at  $600^\circ\text{C}$ ., yielding sodium and carbon (19). However, Hackspill and Schwartz were able to prepare traces of the carbide by heating sodium and carbon under pressure at  $980^\circ\text{C}$ . (20).

Metallic *potassium*, *rubidium*, and *cesium* differ from sodium in that they readily combine with carbon at temperatures below  $70^\circ\text{C}$ ., to form compounds of the type  $\text{MC}_8$ . In the case of potassium, a dark copper-red carbide of the formula  $\text{KC}_4$  and a blue-black carbide of the formula  $\text{KC}_{16}$  are known. The existence of these compounds has been definitely proven by a study of the partial pressure of potassium resulting from their dissociation (16). Furthermore, the "heat of solution" of 1 mole of graphite in an excess of potassium has been determined as 1500 cal. On hydrolysis of the carbides, Fredenhagen and Cadenback (16) were unable to obtain hydrocarbons, pure hydrogen being evolved. Under certain conditions, the potassium content of the potassium carbides did not readily go into solution in water, being held very tenaciously by adsorption or chemical combination.

Of the alkali metals, *lithium* alone readily combines with carbon to form a carbide with acetylenic linkages. The electrothermal reduction of lithium carbonate with carbon yields lithium carbide,  $\text{Li}_2\text{C}_2$  (36). It is interesting to note that the heat required to form 1 mole of lithium carbide by carbon reduction of the oxide is 101.7 Cal. (21), in comparison with the value of 108.0 Cal. for calcium carbide (33)

#### *Alkaline earth metal carbides*

In addition to the usual lime-carbon process, of which Mantell (33) has given a good description, *calcium carbide* may be prepared by carbon reduction of calcium silicates (73), calcium phosphate (54), or calcium sulfate (71). Although calcium carbide has always been the principal industrial source of acetylene (33), its predominant position in this field may eventually be threatened by processes based on the pyrolysis of hydrocarbons (12, 65).

Monobasic calcium acetylide, like the corresponding alkali metal com-

pounds, is precipitated when acetylene is passed into a liquid ammonia solution of the metal. This compound is transformed to calcium carbide on gentle heating (69).

*Barium carbide* may be prepared at 1150°C. in 60 per cent yield by reduction of the oxide with carbon in a stream of methane. The formation of barium hydride ( $\text{BaH}_2$ ) is believed to prevent a higher yield (14). The carbide may also be prepared by reduction of the carbonate with aluminum (30), and by reduction of the oxide, hydrate, or carbonate with coal in a blast furnace (24, 59, 77).

#### *Carbides of aluminum, beryllium, magnesium, and ammonium*

The principal difficulties in the preparation of *aluminum carbide*,  $\text{Al}_4\text{C}_3$ , are due to its volatility (61, 64, 75). At the boiling point, 2270°C., the vapor consists of approximately equal volumes of aluminum and aluminum carbide (48). Slow heating favors the formation of the yellow, crystalline carbide (45, 63). When carbon is heated with porcelain at as low a temperature as 1400°C., a film of aluminum carbide can be detected by x-ray analysis (28). Water reacts with aluminum carbide twenty-three times faster than does deuterium oxide, pure methane and tetradeuteromethane being formed (66).

When *beryllium* oxide is reduced with carbon, the carbide,  $\text{Be}_2\text{C}$ , is formed. Each carbon atom is enclosed by a cube of beryllium atom (figure 1 b); the distance between carbon atoms is 3.06 A.U. and between beryllium and carbon atoms is 1.87 A.U. (58). This compound yields methane on hydrolysis (58). At high temperatures, beryllium has more affinity for copper than for carbon (37).

By reaction of *magnesium* with acetylene in liquid ammonia, the acetylide,  $\text{Mg}_2\text{C}_2 \cdot \text{C}_2\text{H}_2 \cdot 5\text{NH}_3$  has been prepared. Analogous to hydrated magnesium chloride, the compound must be heated under reduced pressure if the monobasic or dibasic acetylides are to be prepared in the pure condition. At atmospheric pressure, as much as 92 per cent of the compound is ammonolyzed to magnesium amide,  $\text{Mg}(\text{NH}_2)_2$  (10). The magnesium acetylides are also readily prepared by treating Grignard reagents with acetylene (18). The electrothermic reduction of magnesium oxide with carbon gives very low yields of the carbide  $\text{MgC}_2$ , metallic magnesium being the principal product (62).

One of the most remarkable of all carbides is formed when dibasic magnesium acetylide is heated above 500°C., the allylide  $\text{Mg}_2\text{C}_3$  being produced (39). At 650°C., the conversion of the acetylide to magnesium, carbon, and magnesium allylide is complete. Unfortunately, magnesium allylide begins to decompose at 600°C., and the yield by this method is only 30 per cent. The hydrolysis of this compound yields pure allylene,

which Novak thoroughly characterized by several methods which included analysis of the silver salt and  $\alpha$ -iodo derivative ( $\text{CH}_3\text{C}\equiv\text{CI}$ ) (38). Since allylene does not react with ammoniacal cuprous chloride, quantitative separation of the hydrocarbon gases was obtained by absorption of the acetylene in this reagent, followed by absorption of the allylene with ammoniacal silver nitrate (39).

By passing hydrocarbon gases over magnesium at  $690^\circ$  to  $760^\circ\text{C}$ ., the maximum yields of magnesium allylide which Novak obtained were as follows: methane, 50 per cent; pentane, 74 per cent; octane, 58 per cent; benzene, 70 per cent; toluene, 2 per cent; xylene, 7 per cent. Furthermore, the optimum temperature for each hydrocarbon was determined. As Novak pointed out twenty-five years ago, allylene prepared by this method should provide a comparatively inexpensive raw material for the preparation of such compounds as propionaldehyde (39).

The non-existence of appreciable quantities of ammonium acetylides in liquid ammonia solutions of acetylene has been inferred from the high electrical resistance of the solution (10). However, this solution readily attacks magnesium (10) and the alkaline and alkaline earth metals (10, 35, 68).

#### *Iron, nickel, cobalt, and manganese carbides*

Iron forms the carbides  $\text{Fe}_3\text{C}$  (23),  $\text{Fe}_2\text{C}$  (3, 17, 22), and probably also  $\text{FeC}$  and  $\text{FeC}_2$  (70). The solubility of carbon in iron is as follows (34):

Temperature ( $^\circ\text{C}$ .)	1220°	1522°	1823°	2122°	2169°	2220°	2271°	2420°
Per cent carbon ...	4.58	5.46	6.59	7 51	8.21	9.6	8 97	8 09

When the solutions were very rapidly cooled, nearly all of the carbon was obtained in combined form (34). By heating iron above  $2600^\circ\text{C}$ ., Vittorf (70) found that as much as 30 per cent of carbon dissolved. In his experiments with synthetic diamonds, Moissan found that very little carbon separated out when boiling, saturated iron-carbon solutions were rapidly cooled (36).

Cementite,  $\text{Fe}_3\text{C}$ , is the most common iron carbide. It has a white silver color. Since it reacts with acids more slowly than iron, a separation from iron may be rather easily effected (34, 36). This carbide is stable above  $700^\circ\text{C}$ ., but slowly decomposes at  $500^\circ\text{C}$ .. (50). The heat of formation is  $-12,300$  cal., the compound being endothermic (76). By the action of carbon monoxide on iron at  $400^\circ\text{C}$ ., cementite is formed; between  $230^\circ$  and  $400^\circ\text{C}$ ., the product is a mixture of cementite and  $\text{Fe}_2\text{C}$ ; below  $230^\circ\text{C}$ ., the product is pure  $\text{Fe}_3\text{C}$  (3).

Cementite is the only carbide of iron whose hydrolysis has been investigated. Under favorable conditions, 40 per cent of the carbon content



may form a mixture of solid and liquid hydrocarbons (34) that are but slightly soluble in ether, and which consist of a large number of compounds of the paraffin and olefin series (35). More or less free carbon is always obtained (50).

*Nickel carbide*,  $\text{Ni}_3\text{C}$ , is best prepared by passing carbon monoxide over heated nickel (2). Very little, if any, free carbon results on hydrolysis (2, 53). This was explained by Schmidt (52) on the basis of the nickel carbide crystal lattice. Each carbon atom is surrounded by a hexagonal prism of six nickel atoms (25) which hydrogenate the carbon atom before it gets a chance to form free carbon (52). The hydrolysis of nickel carbide with 3 *N* hydrochloric acid yields 67 per cent of the carbon as gaseous hydrocarbons, and 33 per cent as liquid hydrocarbons (2). Dilute nitric acid gives nitro compounds (2).

In slightly acid solutions, nickel chloride reacts with calcium carbide to form an acetylide (11).

TABLE 3

*Composition of the gaseous mixture resulting from the hydrolysis of carbides*

CARBIDE	$\text{C}_2\text{H}_2$	$\text{C}_2\text{H}_4$	$\text{CH}_4$	$\text{H}_2$
	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
$\text{ThC}_2$ .....	75.8	3.8	20.9	
$\text{CeC}_2$ .....	47.6	5.8	29.4	17.1
$\text{UC}_2$ .....	0.17-0.72	5.16-6.17	78.05-80.6	13.52-15.01

The order of stability of the carbides of the iron group is cobalt, iron, and nickel (5, 49).

By means of x-ray analysis, Jacobson and Westgren (25) have proven the existence of *manganese carbides* of the compositions  $\text{Mn}_4\text{C}$ ,  $\text{Mn}_3\text{C}$ , and  $\text{Mn}_7\text{C}$ . Fischer and Baugert (15) obtained in addition  $\text{Mn}_5\text{C}_2$ . When  $\text{Mn}_3\text{C}$ , the carbide obtained by the electrothermal reduction of  $\text{MnO}_2$ , is hydrolyzed, the gases evolved consist of 2.5 per cent of unsaturated hydrocarbons, 45 per cent of saturated hydrocarbons, and 52.5 per cent of hydrogen (36). The carbide  $\text{Mn}_3\text{C}$  is ferromagnetic, has a hardness between 1 and 2 on the Mohr scale (72), and readily decomposes water (15).

#### *Miscellaneous carbides*

By reduction of thorium dioxide with carbon, *thorium carbide* is obtained as large, yellow, transparent crystals melting at  $2500^\circ\text{C}$ . (44). Table 3 gives the volume composition of the gaseous mixture resulting from its hydrolysis (36).

The rare earth carbides are isomorphous with those of the calcium group (78). *Cerium carbide* readily reacts with water (29), evolving a gas whose composition (36) is given in table 3.

*Uranium* forms the carbide  $UC_2$  (51), which water slowly decomposes at room temperature (34). On hydrolysis, one-third of the carbon is evolved in the gas mixture whose composition is given in table 3 (36). The rest of the carbon, about two-thirds of the total quantity, forms liquid and solid hydrocarbons (36). Uranium carbide gives a larger quantity of liquid and solid hydrocarbons than any other carbide.

Durand found that calcium carbide reacted with aqueous solutions of several metallic salts to form acetylenic carbides. Among the carbides he claimed to have prepared in this manner were  $Cu_2C_2$ ,  $CuC_2$ ,  $AgC_2$ ,  $Hg_2C_2$ ,  $HgC_2$ , and  $PbC_2$  (11). Each of these carbides is soluble in mineral acids (34). The precipitation of the explosive silver carbide has long been the basis of an analytical method for acetylene determination (40, 41).

Carbides of zinc, cadmium, antimony, and bismuth are unknown.

#### UNSOLVED PROBLEMS

1. Apparently the only information available concerning magnesium allylide is Novak's work (38, 39), which was done twenty-five years ago. His low yields when toluene and xylene were used to prepare the carbide are difficult to explain. Moreover, the accuracy of the analytical methods which he used is in doubt as a result of recent work (40, 41). Confirmation of his results and further investigation of this interesting carbide are needed.

2. The hydrolysis of mixtures of carbides is a subject of considerable theoretical interest.

3. No analyses have yet been made of the hydrolysis products of iron carbides other than  $Fe_3C$ , or of manganese carbides other than  $Mn_3C$ .

4. Very little work has been done on the effects of temperature, pH, salt concentrations, and contact agents on the hydrolysis products of the carbides of uranium, manganese, iron, nickel, and cobalt.

5. The decomposition of carbides with reactants other than water under higher temperatures and pressures offers a possible synthesis of many new compounds.

The hydrolysis of carbides is an interesting subject that should be worthy of further investigation. From both an industrial and a purely scientific standpoint, this field should amply reward the research worker.

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# THE HEAT OF DISSOCIATION OF THE CARBON MONOXIDE MOLECULE AND THE HEAT OF SUBLIMATION OF CARBON<sup>1</sup>

G. HERZBERG

*University of Saskatchewan, Saskatoon, Canada*

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There has recently been a great deal of discussion on the value of the heat of dissociation of the carbon monoxide molecule,  $D(\text{CO})$ . Various widely diverging values have been given as more or less definite for this quantity by different investigators. All these values have been obtained by spectroscopic methods. The discrepancies in the case of carbon monoxide seem to throw a rather unfavorable light on the reliability of these spectroscopic methods, and the non-spectroscopist may even doubt their accuracy and reliability in other cases where the spectroscopic values claim to be perfectly certain and have been generally accepted. In the first part of this paper we shall, therefore, summarize the various spectroscopic methods, emphasizing under what conditions they supply reliable values for the heats of dissociation,  $D$ . In the second part, these methods will be applied to carbon monoxide as far as possible. The various spectroscopic values for  $D(\text{CO})$  proposed in the literature will be discussed, possible reasons for the discrepancies will be pointed out, and a value which seems most probable to the author will be given.

The value of  $D(\text{CO})$  is rather important in the discussion of many chemical problems. Particularly the heat of sublimation of carbon into normal atoms  $L_1$  may be derived from  $D(\text{CO})$ .  $L_1$  in its turn is necessary for the calculation of atomic heats of formation and bond energies of carbon compounds. Therefore a discussion of the heat of sublimation of carbon is added, as well as a brief discussion of the dissociation energy of the CN radical, which also may be derived from  $D(\text{CO})$ .

## I. SPECTROSCOPIC METHODS FOR THE DETERMINATION OF HEATS OF DISSOCIATION OF DIATOMIC MOLECULES

In forming a molecule the atoms may be brought together in any of their excited states, including of course the normal state. From each of

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the combinations of the excited atoms in general *several* electronic states of the molecule arise. The different electronic states belonging to the same combination of atomic states have different potential energy curves, some with a minimum of potential energy (stable states) and some without it (unstable repulsive states). The difference in energy of the zero vibrational level of an electronic state and the asymptote of the potential curve is the dissociation energy of that state. The energy corresponding to the asymptote is also called the *dissociation limit*. There are as many different dissociation limits as there are combinations of the different states of the two atoms. The distance of the lowest dissociation limit which corresponds to dissociation into normal atoms from the ground state of the molecule is called the *dissociation energy of the molecule*. This is the quantity in which the chemist is most interested. Usually (but not necessarily) the ground state of the molecule is derived from normal atoms, i.e., the dissociation energy of the ground state is the dissociation energy of the molecule.

There are always two steps in the spectroscopic determination of this quantity: (A) the determination of one or preferably more of the dissociation limits of the molecule; (B) the determination of the products of dissociation, i.e., of the states in which the atoms are at the dissociation limits which have been found. The discrepancies which occur in the literature are mostly caused by a mistake or ambiguity in the second step.

#### A. Determination of dissociation limits

There are four possible ways of performing step A, i.e., of determining dissociation limits from band spectra.

*Method a.* The oldest method, due to Franck, is that of the *convergence limits* of band series. If the molecule goes over from the vibrationless ground state to the various vibrational levels of an upper electronic state, a series of bands is observed in the absorption spectrum, somewhat as in figure 1.

The distance of successive bands decreases towards shorter wave lengths until it reaches the value zero at a certain limit, the convergence limit, where a continuous spectrum follows to still shorter wave lengths. This continuous spectrum means, as has been rigorously proved both experimentally and theoretically, a dissociation of the molecule. The beginning of the continuous spectrum, i.e., the convergence limit, corresponds to the beginning of dissociation, i.e., the dissociation limit.

Figure 2 shows the potential curves of the upper and lower state in a case like this. Absorption of light in the continuous region means dissociation with a certain amount of kinetic energy, corresponding in magnitude to the distance from the convergence limit.

If a convergence limit like this is actually observed for a certain molecule, at once a very accurate and reliable value for the corresponding dissociation limit can be given.<sup>2</sup> This method has been applied very successfully to  $I_2$ ,  $O_2$ ,  $H_2$ , and others. Unfortunately, many diatomic molecules do not exhibit a suitable absorption spectrum, therefore other methods have to be applied to them.

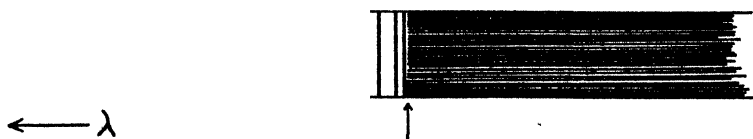


FIG. 1. Band series with convergence limit and continuous spectrum (schematically)

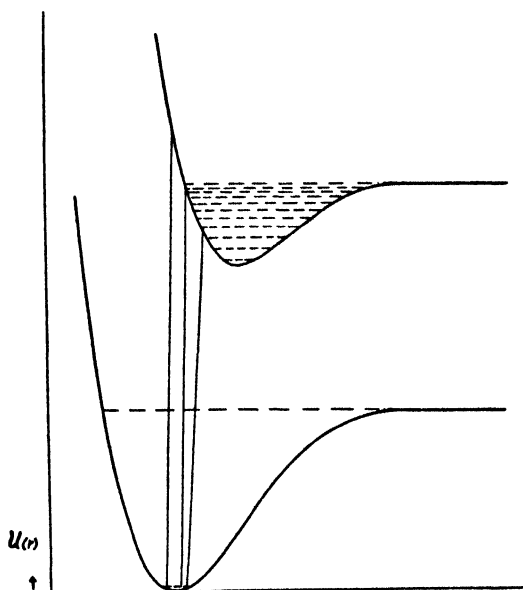


FIG. 2. Potential curves for figure 1

*Method b.* It often happens that not the complete series of absorption bands up to the point of convergence and the continuum are observed, but

<sup>2</sup> There is a remote possibility that under certain very special circumstances the potential curve of the upper state has a maximum before approaching the asymptote. In that case the observed limit in the absorption spectrum would correspond to an energy greater than the dissociation limit. So far no such case has been observed with certainty. Also, it would be possible to distinguish it from the ordinary case, figure 2, so that we need not discuss it here.



only the first few bands corresponding to the first vibrational levels of the upper state. Similarly in emission usually only transitions between the lower vibrational levels are observed. The reason for this is given by the Franck-Condon principle (24, 37). As the distance between the vibrational levels, i.e., the distance of the corresponding bands in general decreases regularly, Birge and Sponer have proposed to *extrapolate* the series of the observed quanta to zero and then add all the vibrational quanta to obtain the heat of dissociation of the state in question. The advantage of this procedure is that it may be applied to any electronic state of a molecule for which a number of vibrational levels are known.

However, it has been found in recent years that the results of this method are often not at all accurate. In some cases the true values obtained by other methods deviate from the extrapolated values by as much as 40 per cent. The error is much smaller if the extrapolation is comparatively short. In most of the cases which have been tested so far the extrapolated value was higher than the true value, so that one may say that the extrapolations according to Birge and Sponer, in general give an upper limit for the heat of dissociation of a particular electronic state of the molecule, whereas, of course, the sum of the actually observed vibrational quanta always gives a lower limit for it. The knowledge of this lower limit, which is quite definite, may sometimes be of help in the discussion of dissociation energies.

*Method c.* Sometimes in absorption only a continuous spectrum is observed. This either corresponds to the transitions to the continuous part of a stable electronic level, the discrete part being not observed owing to the Franck-Condon principle, or to the transition into an unstable repulsive electronic state. Evidently the long wave length limit of this continuum gives a definite upper limit for the dissociation energy of the molecule.<sup>3</sup> But an accurate value for the dissociation limit cannot be derived because the point of convergence cannot be located. In fact the upper limit derived from the long wave length limit of the continuum may be and in some cases has actually been found to be appreciably higher than the true value.

Instead of using the continuous absorption as an indication of dissociation, Terenin has used the occurrence of fluorescence of the atoms produced if the dissociation takes place into excited atoms. As this is not important for the discussion of carbon monoxide we shall not deal with this method in more detail.

*Method d.* A method which under certain conditions also gives very

<sup>3</sup> This refers to adsorption at sufficiently low temperatures, where absorption due to molecules in higher vibrational levels of the ground state does not interfere.

reliable results, just as method a, is the determination of dissociation limits by *predissociation*.<sup>4</sup>

Predissociation was discovered by V. Henri when he investigated the absorption spectra of a number of molecules. He found in some cases that though the absorption bands are quite sharp at longer wave lengths, they become diffuse more or less suddenly at a certain point and sometimes get sharp again at shorter wave lengths.

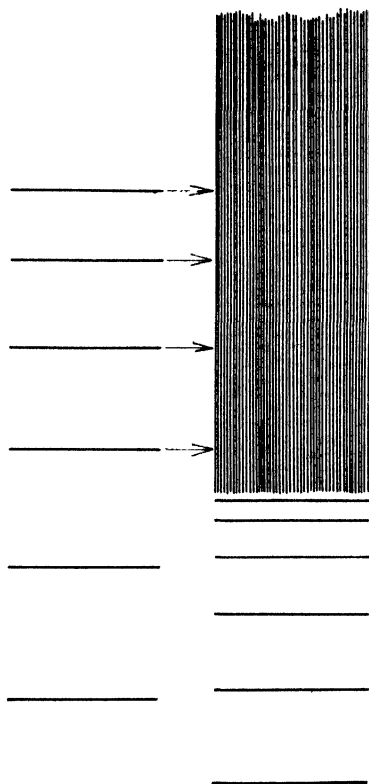


FIG. 3 Radiationless transitions (predissociation) from a discrete to a continuous state

This diffuseness was shown by Born, Franck, Kronig, and others, to be due to an instability of the molecule. Namely, if the upper level of the bands has a larger energy than a dissociation limit of the molecule, it is overlapped by the continuous term spectrum which extends beyond this dissociation limit, as indicated in figure 3. Owing to quantum-mechanical

<sup>4</sup> For a more complete discussion of this, see the author's review on predissociation (17).

resonance, there is then a certain probability that the molecule performs a radiationless transition (indicated by horizontal arrows in figure 3) from the discrete excited state to the continuous term spectrum, and this under certain conditions, as shown by the theory, produces the diffuseness which is observed. It follows immediately that the *predissociation limit*, i.e., the beginning of the diffuseness of the bands, gives an upper limit to the dissociation energy of the molecule.

It has been shown experimentally, first by Bonhoeffer and Farkas, that a dissociation of the molecule really does occur if light of the diffuse absorption bands is absorbed. Moreover, it was found, as is to be expected on this theory of radiationless dissociation, that bands which have the diffuse states as upper states do not occur in emission, whereas the other bands of the same system do. Thus there are three possible tests for predissociation: diffuseness of absorption bands, actual dissociation, and quenching of emission bands.

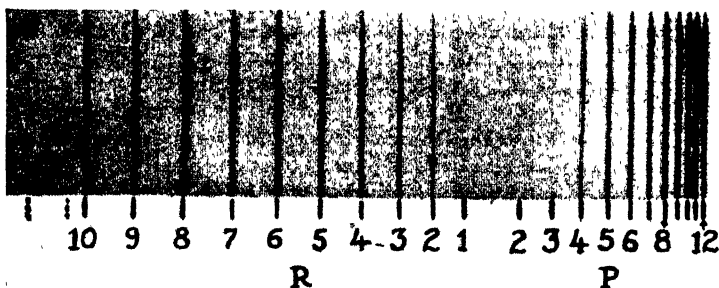


FIG. 4. Breaking off (predissociation) in the CaH band at 3533.6 Å  $\mu$ , according to Mulliken

In order to produce a detectable diffuseness in the absorption bands, the radiationless transition probability must be at least ten to one-hundred times larger than the transition probability for radiation, whereas to produce a detectable quenching, it is sufficient that the two transition probabilities be of about the same magnitude.<sup>4</sup> Therefore, quenching of emission bands is a much more sensitive test for predissociation. Also, it can be applied to detect predissociation in electronic states of a molecule which cannot be investigated by absorption.

The quenching of emission bands due to predissociation is usually detected by an abrupt breaking off of the band spectrum at a certain value  $a$  of the vibrational quantum number,  $v'$ , of the upper state. Bands having  $v' > a$  do not occur at all or only much weaker than those with  $v' \leq a$ . In many cases if the rotational fine structure of the bands is resolved, it is even found that the break occurs between successive rotational levels of

the last vibrational level  $v' = a$ . Figure 4 gives as an example an emission band of CaH, where the breaking off in the two branches (on the extreme left and extreme right) can be clearly seen. Lines with the rotational quantum number of the upper state  $K' > 11$  are completely missing, whereas lines with  $K' \leq 11$  have the ordinary intensity. In some cases, only a sudden drop in intensity is observed instead. Evidently the predissociation limit can be fixed with considerable accuracy if such a breaking off of the rotational fine structure is observed.

In principle, predissociation in an excited state of a molecule is possible as soon as its energy is larger than the energy necessary to dissociate the molecule into normal atoms. But, just as for transitions with radiation, there are also selection rules for radiationless transitions, and in consequence of that in some cases a predissociation may not be possible into normal atoms, but only into excited atoms.

In order to formulate the selection rules, it has to be remembered that the unstable state into which the radiationless transition occurs is nevertheless a molecular state, also characterized by the various molecular quantum numbers and symmetry properties. According to Kronig, a radiationless transition can only occur between states which have the same symmetry properties, and for which  $\Delta S = 0$ ,  $\Delta J = 0$ , and  $\Delta \Lambda = 0$  or  $+1$  or  $-1$ . The rule  $\Delta S = 0$  is the ordinary intercombination rule, which holds to the same extent as for ordinary transitions with radiation. The other rules will not be discussed here in detail because we do not need them for the following.

In addition to the Kronig rules, the Franck-Condon principle has to be considered.<sup>4</sup> In consequence of that, in general predissociation will only occur if the potential curves of the two states involved intersect. The point of intersection may be (a) at about the same height as the asymptote of the state into which predissociation takes place or (b) below it or (c) above it. This is shown in figure 5. In the cases a and b, a predissociation, i.e., a going over from potential curve  $\alpha$  to  $\alpha'$  will occur as soon as the energy is larger than that of the asymptote. Consequently the predissociation limit is equal to the dissociation limit of the molecule. However, in case c, where the point of intersection is above the asymptote, predissociation can only occur for vibrational levels above this point of intersection.<sup>5</sup> Therefore, in this case the predissociation limit is larger than the corresponding dissociation limit. Only if it is possible to exclude this case c for an observed predissociation, can a dissociation limit be

<sup>5</sup> As we have to do with motions of heavy nuclei, the quantum-mechanical tunnel effect produces a detectable going over from  $\alpha$  to  $\alpha'$  in figure 4c only immediately below the top of the potential hill formed by the two curves. This can be neglected here. (Cf. reference 18.)

accurately determined from the predissociation limit. In all other cases, predissociation limits only give upper limits for dissociation limits.

The above-mentioned possibility of excluding case c exists if a breaking off of the rotational levels is observed not only in one but in two or more successive vibrational levels (18, 19a). Evidently, if in the last vibrational level  $v' = a$  the breaking off occurs for a low value of the rotational

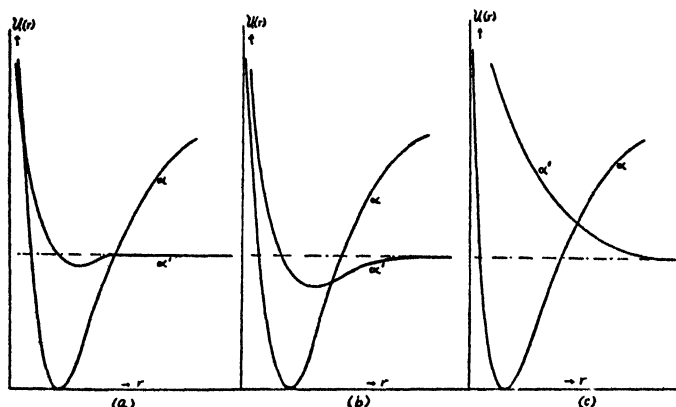


FIG. 5. The three different cases of predissociation

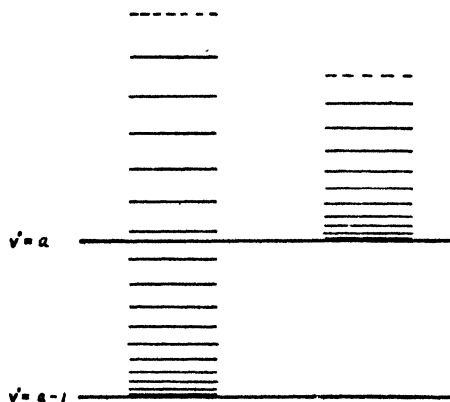


FIG. 6. Breaking off in two successive vibrational levels

quantum number  $K$  there may also be a breaking off in the level  $v' = a - 1$  at a correspondingly higher  $K$  value, as indicated in figure 6. Owing to the influence of the centrifugal force, the breaking off occurs at a slightly higher energy in the level  $v' = a - 1$  than in the level  $v' = a$ . Theory shows that only if this difference in energy is small compared to the difference of the pure rotational energies of the two levels, does case c not

apply, i.e., the predissociation limit is very near to the dissociation limit. In fact, even a lower limit for the latter may be obtained in this case, so that it is included between two rather close limits. Under these conditions, but only then, is it possible to derive very reliable and accurate values for dissociation limits from predissociation data. In all other cases the latter give only upper limits for dissociation limits.

If the intensity drop occurs only for a few consecutive fine-structure lines in emission, it is, except in special cases, due to *perturbation*, not ordinary predissociation. Perturbations arise by a sort of resonance if two discrete levels of the molecule have very nearly the same energy. This leads to a shift of the energy levels from their original position and, at the same time, to a change in intensity of the corresponding fine-structure lines. If, therefore, the lines with low intensity at the same time have not their regular position, the drop in intensity has nothing to do with predissociation. But sometimes, e.g., in some  $N_2$  bands (7), an intensity drop for a few lines is observed without corresponding frequency shift. This was explained by Ittmann (23) as *accidental predissociation*, i.e., a perturbation for which the perturbing term is a predissociating term at the same time. In this case the intensity drop, as for ordinary predissociation, is due to a dissociation of the molecule, not however by a direct radiationless transition to the unstable state, but by first going over to another discrete state which then predissociates. This explains at once the fact that an intensity drop occurs only for very few consecutive rotational states, just as for ordinary perturbations but without noticeable frequency shift. Though this is so far the only experimental proof for accidental predissociation, it seems fairly safe to assume the correctness of this interpretation of intensity drops for a few consecutive lines without frequency shift. It is evident from the foregoing that an observed accidental predissociation gives an upper limit for a dissociation limit but not more, whereas ordinary perturbations of course have nothing to do with dissociation limits.

### *B. Determination of the products of dissociation*

The values for the dissociation limits obtained by any of the methods a, b, c, or d in general correspond to dissociation into more or less excited atoms. In order to determine the dissociation energy of the molecule, the state of excitation of the atoms produced at the observed dissociation limit has to be determined. If that is not possible, the observed dissociation limits, even if they are accurate, are only upper limits for the dissociation energy of the molecule which is smaller by the excitation energy of the products of dissociation (cf. figure 2).

Information about the products of dissociation for a certain dissociation limit may be obtained in three ways:

(1). By comparing its energy with that of other dissociation limits of the same molecule (or the corresponding molecule ion). Evidently the differences in energy of the various dissociation limits must equal the energy differences of the two free atoms forming the molecule.

(2). By application of the Wigner-Witmer *correlation rules* (30). These rules give the number and type of the molecular terms which can arise from each combination of terms of the two atoms forming the molecule, e.g., an atom in a  $^2S$  state and one in a  $^3P$  state can give only the molecular states  $^2\Sigma$ ,  $^2\Pi$ ,  $^4\Sigma$ ,  $^4\Pi$  and no others; two equal atoms both in a  $^3P$  state give the molecular states  $^1\Sigma_g^+$ ,  $^1\Sigma_g^+$ ,  $^1\Sigma_u^-$ ,  $^1\Pi_g$ ,  $^1\Pi_u$ ,  $^1\Delta_g$ ,  $^3\Sigma_u^+$ ,  $^3\Sigma_u^+$ ,  $^3\Sigma_g^-$ ,  $^3\Pi_u$ ,  $^3\Pi_g$ ,  $^3\Delta_u$ ,  $^5\Sigma_g^+$ ,  $^5\Sigma_g^+$ ,  $^5\Sigma_u^-$ ,  $^5\Pi_g$ ,  $^5\Pi_u$ ,  $^5\Delta_g$  and similarly in other cases. The Wigner-Witmer rules are derived from pure symmetry considerations and are therefore strictly valid.<sup>6</sup>

(3). In special cases by observation of atomic fluorescence when the molecule has been irradiated with light that produces dissociation of the molecule into one excited and one normal atom. The emitted atomic line of course indicates the excitation energy of the atom on dissociation. This method was first applied by Terenin. It will not be used in the following considerations.

For a better understanding of methods 1 and 2 let us consider two examples, the determination of the heats of dissociation of  $O_2$  and  $N_2$ .

In  $O_2$  a convergence limit was observed in the absorption spectrum at 1770 Å.U., corresponding to an energy of 7.01 volts.<sup>7</sup> There are three low-lying terms of the oxygen atom (8, 22),  $^3P$  (ground state),  $^1D$  (1.957 volts),  $^1S$  (4.168 volts), which have to be considered as dissociation products at the limit 7.01 volts.<sup>8</sup> The two oxygen atoms may therefore be in the states  $^3P + ^3P$  or  $^3P + ^1D$  or  $^3P + ^1S$  or  $^1D + ^1D$  or  $^1D + ^1S$  or  $^1S + ^1S$ . The upper state of the absorption bands which lead to the convergence is a  $^3\Sigma_u^-$  state, as shown by the fine-structure analysis. Such a state, according to the Wigner-Witmer rules, cannot dissociate into two normal  $^3P$  atoms (see the previous example) (15). Similarly the three combinations  $^1D + ^1D$ ,  $^1D + ^1S$ , and  $^1S + ^1S$  are excluded because they do not give triplet states at all. The two remaining possibilities,  $^3P + ^1D$  and  $^3P + ^1S$ , would give  $7.01 - 1.96 = 5.05$  volts and  $7.01 - 4.17 = 2.84$

<sup>6</sup> For heavy molecules sometimes Hund's case *c* applies. The adaption of the Wigner-Witmer rules to this case has been given by Mulliken (30).

<sup>7</sup> This is the new value given by Knauss and Ballard (25), which is based on spectrograms of much higher dispersion than the previous value, 7.05 volts.

<sup>8</sup> The next highest term of oxygen is 9.1 volts above the ground level. If one of the dissociation products were in that state, a negative value for *D* would result.

volts, respectively, for the dissociation energy of oxygen. The latter value is smaller than the sum of the observed vibrational levels of the ground state, 3.4 volts. Thus the value 5.05 volts = 116.4 kg-cal. per mole for  $D(\text{O}_2)$  follows without ambiguity. In fact, a second convergence limit was later found (19) at 5.09 volts, corresponding to dissociation into normal atoms  $^3P + ^3P$ . The distance between the two convergence limits is 1.92 volts, which is equal to the excitation energy of the  $^1D$  level within the splitting of the  $^3P$  ground state.<sup>9</sup> Thus the previous conclusion that the upper convergence limit corresponds to a dissociation into  $^3P + ^1D$  is confirmed and the reliability of the method shown. The spectroscopic  $D(\text{O}_2)$  value is now absolutely certain, and much more accurate than any thermal or chemical value hitherto obtained.

For  $\text{N}_2$  predissociation has been observed in the  $C^3\Pi_u$  and in the  $B^3\Pi_g$  states (16, 20, 7, 40). By the method indicated previously the predissociation in  $C^3\Pi_u$  leads to a reliable value for a dissociation limit at 12.08 volts (16, 20, 7), whereas from the predissociation in the  $B^3\Pi_g$  state it is only possible to give an upper limit of 9.79 volts for the corresponding dissociation limit. The low-lying states of the nitrogen atom are  $^4S$  (ground state),  $^2D$  (2.368 volts),  $^3P$  (3.553 volts). As possible products of dissociation we have  $^4S + ^4S$  or  $^4S + ^2D$  or  $^4S + ^3P$  or  $^2D + ^2D$  or  $^2D + ^3P$  or  $^3P + ^3P$ . A closer examination of the lower predissociation at 9.79 volts shows that the unstable state producing the predissociation must be a  $\Pi$  or a  $\Delta$  state,<sup>10</sup> a state which, according to the Wigner-Witmer rules, cannot be obtained from  $^4S + ^4S$ . The other possibilities for the dissociation products at this limit give the following upper limits for  $D(\text{N}_2)$ :  $\leq 7.42$  or  $\leq 6.24$  or  $\leq 5.05$  or  $\leq 3.87$  or  $\leq 2.68$  volts. The last three values are definitely excluded by the fact that the energy of the last observed vibrational level of the ground state has the energy 5.5 volts. Also the value  $D(\text{N}_2) \leq 6.24$  volts seems to be extremely improbable on this basis, so that we have  $D(\text{N}_2) \leq 7.42$ . A more accurate value can be obtained by making use of the upper predissociation in the  $C^3\Pi_u$  state which gave an exact value for a dissociation limit (=12.08 volts). If  $D(\text{N}_2)$  is between 7.42 and 6.24 volts the upper predissociation must correspond to a dissociation into  $^2D + ^2D$ , so that we have  $D(\text{N}_2) = 12.08 - 2 \times 2.368 = 7.345$  volts = 169.3 kg-cal. per mole (21; 20). The remote

<sup>9</sup> The difference between the distance 1.92 volts of the two dissociation limits and the energy difference 1.96 volts of the ground state  $^3P_2$  of the oxygen atom and the  $^1D$  state is evidently due to the fact that at the lower dissociation limit not two normal  $^3P_2$  atoms are obtained, but  $^3P_2 + ^3P_0$  or  $^3P_1 + ^3P_0$ , which corresponds to an energy difference of 0.03 or 0.05 volt, respectively.

<sup>10</sup> A  $\Sigma$  state could, so to speak, only predissociate half of the  $B^3\Pi_g$  state, and in consequence of that not all of the three branches of a band could show the breaking off as they actually do.



possibility that predissociation at 12.08 volts takes place into  $^3D + ^3P$  and therefore that  $D(N_2) = 6.18$  volts is completely ruled out by further data on  $N_2$ , which we are not going to discuss here (31). Thus the above value for  $D(N_2)$  is also quite definite and very accurate ( $\pm 0.005$  volt).

## II. APPLICATION TO THE CARBON MONOXIDE MOLECULE

Turning now to the carbon monoxide molecule, we first discuss step A, i.e., the determination of dissociation limits. So far no convergence limit is known for carbon monoxide. Extrapolations of the vibrational levels

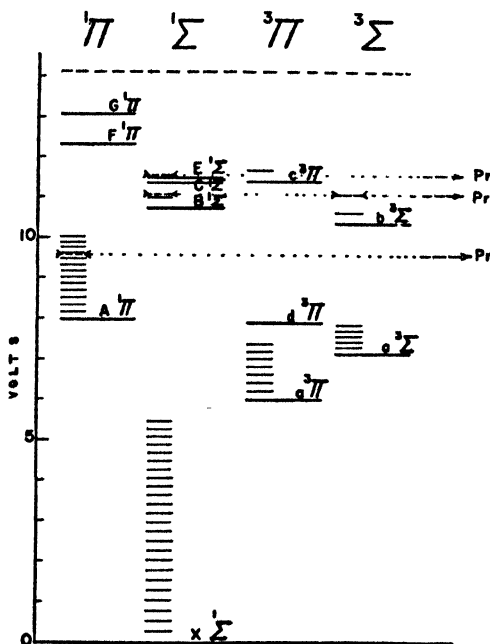


FIG. 7. Energy level scheme of carbon monoxide

of several electronic states have been made in previous years, but, as pointed out above, no reliable  $D$  values can be expected from them. It could, however, be concluded that  $D(CO)$  is comparatively large, of the order of 10 volts.

Most of the recent discussion of  $D(CO)$  is based on predissociation data. Predissociation has been found in four different electronic states of the molecule. The energy level diagram of the carbon monoxide molecule is given in figure 7. The points of predissociation are indicated by "Pr."

The first to discover a predissociation of the carbon monoxide molecule were Coster and Brons (6). They found a sudden drop of intensity in

the 0-1 Ångström band ( $B^1\Sigma \rightarrow A^1\Pi$ ) at  $K' = 38$ . From their published photometer curve this sudden decrease in intensity can be very clearly seen. All the following lines have a much smaller intensity than those before the break. As they do not, however, vanish completely, the radiationless transition probability for some reason is rather low. Schmid and Gerö (34) found a second breaking off in the  $v' = 1$  level of the  $B^1\Sigma$  state at  $K' = 18$ . From this the corresponding dissociation limit can be calculated in the same way as in the case of  $N_2$  previously mentioned (cf. 32). A value of  $89,620 \pm 50 \text{ cm.}^{-1} = 11.054 \text{ volts}$  is obtained.<sup>11</sup>

Schmid and Gerö (9, 35, 12) found a second predissociation in the  $v' = 1$  and  $v' = 0$  levels of the  $b^3\Sigma$  state (upper state of the third positive group). It turns out that this predissociation belongs to the same dissociation limit, so that it need not be discussed further.<sup>12</sup>

A third predissociation was found in the  $v = 0$  level of the  $C^1\Sigma$  state by Schmid and Gerö (36, 33). The energy of this predissociation limit is  $93,550 \text{ cm.}^{-1} = 11.538 \text{ volts}$ . As in this case predissociation is only observed in one vibrational level, the value given represents only an upper limit for the corresponding dissociation limit.

Fourthly, predissociation has been found in the  $A^1\Pi$  state of carbon monoxide. At first Brons (4) thought that he had located a predissociation in the  $v = 10$  level of this state at 9.66 volts above the ground state. But the unreality of this predissociation was soon proved by Gerö (10). According to him the apparent sudden intensity decrease observed by Brons is due to an ordinary perturbation and insufficient exposure time. However, Gerö (11) found another predissociation in the same band system for bands with  $v' = 9, 8$ , and 7. From this he derives in the manner described above a dissociation limit at  $77,497 \pm 44 \text{ cm.}^{-1} = 9.558 \text{ volts}$ . The intensity drop in the 9-18 band reproduced by Gerö is only slight and extends only over two or three successive rotational lines. This suggests that it may not be an ordinary predissociation but a case of accidental predissociation (cf. above) or even of ordinary perturbation. The same may be true for the drop in the levels  $v' = 8$  and 7, which has only been observed in the R branches of two and one bands respectively. To the writer it seems most probable that we have here a case of accidental predissociation, and that therefore the above value is only an upper limit for the corresponding dissociation limit. But the other two possibilities—ordinary predissociation and ordinary perturbation—have also to be considered. The former would mean that 9.558 volts is a real dissociation

<sup>11</sup> This is the value given by Gerö (11).

<sup>12</sup> Lessheim and Samuel (26) have used the fact that no higher vibrational levels are observed in the  $b^3\Sigma$  state to derive an upper limit for  $D(\text{CO})$ , but have not taken account of the observed amount of rotational energy.

limit, whereas the latter would mean that there is no dissociation limit at this energy.

We have thus to deal with the three limits:  $93,550 \text{ cm.}^{-1} = 11.538 \text{ volts}$ ,  $89,620 \text{ cm.}^{-1} = 11.054 \text{ volts}$ , and  $77,497 \text{ cm.}^{-1} = 9.558 \text{ volts}$ , of which the first is only an upper limit for a dissociation limit, the second is equal to a dissociation limit, and the third probably is only an upper limit for a dissociation limit, but may also be equal to it or even may not be real.

As we have the most definite data about the predissociation at 11.054 volts, and as this is equal to a dissociation limit, it seems best to start the discussion of the products of dissociation with it.

TABLE 1

*D(CO), L, and D(CN) values for different assumptions about the products of dissociation at the carbon monoxide dissociation limit, 11.054 volts*

DISSOCIATION PRODUCTS AT 11 054 VOLTS		ATOMIC EXCITATION ENERGY*		D(CO)			L <sub>1</sub>	D(CN)	
Carbon	Oxygen	cm. <sup>-1</sup>	Volts	cm. <sup>-1</sup>	Volts	kg-cal.	kg-cal.	Volts	kg-cal.
<sup>3</sup> P	<sup>3</sup> P	0	0	89,620	11 054	254 8	169 2	7 87	181 4
<sup>1</sup> D	<sup>3</sup> P	10,192	1 257	79,428	9 797	225 8	140 2	6 61	152 4
<sup>3</sup> P	<sup>1</sup> D	15,868	1 957	73,752	9 097	209 7	124 1	5 91	136.3
<sup>1</sup> S	<sup>3</sup> P	21,647	2 670	67,973	8 384	193 3	107 7	5 20	119 9
<sup>1</sup> D	<sup>1</sup> D	26,060	3 214	63,560	7 840	180 7	95 1	4 66	107 3
<sup>3</sup> P	<sup>1</sup> S	33,793	4 168	55,827	6 886	158 7	73 1	3 70	85 3
<sup>5</sup> S	<sup>3</sup> P	34,994	4.32	54,626	6.738	155 3	69 7	3 55	81 9
<sup>1</sup> S	<sup>1</sup> D	37,515	4 627	52,105	6 427	148 1			
<sup>1</sup> D	<sup>1</sup> S	43,985	5 425	45,635	5.629	129 8			
<sup>5</sup> S	<sup>1</sup> D	50,862	6.273	38,758	4.781	110 2			
<sup>1</sup> S	<sup>1</sup> S	55,440	6 838	34,180	4 216	97 2			
<sup>5</sup> S	<sup>1</sup> S	68,787	8.484	20,833	2 570	59 2			

\* The lowest component of the <sup>3</sup>P terms has always been chosen.

The lowest states of the oxygen atom are <sup>3</sup>P (ground state), <sup>1</sup>D (1.957 volts), <sup>1</sup>S (4.168 volts); those of the carbon atom, <sup>3</sup>P (ground state), <sup>1</sup>D (1.257 volts), <sup>1</sup>S (2.670 volts) and <sup>5</sup>S (4.32 volts, not yet observed; the value given was theoretically calculated by Bacher and Goudsmit (2)). Combining each of these states of the carbon atom with each of the states of the oxygen atom gives twelve possibilities as dissociation products at the 11.054 volts dissociation limit. These are given<sup>13</sup> in the order of their energy in the first two columns of table 1. The next two columns give the excitation energy above the normal state <sup>3</sup>P + <sup>3</sup>P in cm.<sup>-1</sup> and volts. In order to get D(CO) the excitation energy of the dissociation products has

<sup>13</sup> A similar but less complete table has also been given by Goldfinger, Lasareff, and Rosen (14).

to be subtracted from the energy of the dissociation limit, 11.054 volts. The resulting  $D(\text{CO})$  values corresponding to the dissociation products of columns 1 and 2 are given in columns 5, 6, and 7 in  $\text{cm}^{-1}$ , volts, and  $\text{kg-cal. per mole}$ . Of these twelve possible values for  $D(\text{CO})$  one has to try to exclude eleven in order to come to a definite value for this quantity.

In the ground state of carbon monoxide twenty-five vibrational levels have been observed so far, the highest one having an energy of about  $45,000 \text{ cm}^{-1} = 5.6 \text{ volts}$ . This is definitely a lower limit<sup>14</sup> for  $D(\text{CO})$ . In fact, considering the slow and quite regular decrease of the observed vibrational quanta (from 2142.1 to  $1551.5 \text{ cm}^{-1}$ ), it seems safe to exclude the last five values of the table so that now seven possible values for  $D(\text{CO})$  ranging from 11.054 to 6.738 volts, remain to be discussed. Nearly all of these values have at some time or other been proposed for  $D(\text{CO})$  in the literature.

In order to come to a decision we try to use the other two predissociation limits at 11.538 and 9.558 volts. As the former is only an upper limit, its difference from the limit at 11.054, which is 0.484 volts, must be an upper limit to the difference of excitation energies of the products of dissociation at these two limits. The only differences of the excitation energies in the table which fulfil this condition are 0 or 0.15 or 0.31. The first would mean that the two predissociation limits, 11.054 and 11.538, lead to the same products of dissociation, i.e., the dissociation limits would be identical and nothing could be derived about the dissociation products. The second value would mean a dissociation into  $^3P + ^1S$  at 11.054, and the third a dissociation into  $^5S + ^3P$ . As no decision between these three possibilities can be given, the predissociation limit at 11.538 does not lead to any selection of the seven proposed values for  $D(\text{CO})$ . It is compatible with any of them.<sup>15</sup>

In using the predissociation at 9.558 volts discovered by Gerö, in order to come to a selection, the three possibilities mentioned above have to be considered: (1) that there is a real predissociation in three succeeding levels leading to a definite dissociation limit, as assumed by Schmid and Gerö (36a); (2) that the intensity drops observed by Gerö are due to accidental predissociation; (3) that they are due to ordinary perturbations.

(1). If 9.558 is a real dissociation limit just as 11.054, the difference between the two, 1.496 volts, must be exactly equal to an energy difference

<sup>14</sup> This conclusion would be wrong if the ground state would not dissociate into normal atoms. But there is no indication whatsoever for that.

<sup>15</sup> Schmid and Gerö (36), as well as Brons (4), have assumed that the difference 0.484 of the two predissociation limits corresponds to the energy difference 0.544 of  $^1D + ^1D$  and  $^1S + ^3P$ , and have thereby thought to confirm the value  $D(\text{CO}) = 8.385 \text{ volts}$ . As, however, 0.484 is an upper limit for the energy difference this conclusion is not correct (cf. Herzberg (19a)).

of the two atoms, carbon and oxygen. In fact, the difference between  $^3P + ^1S$  and  $^1S + ^3P$  is 1.498, which is indeed a very close fit, well within the accuracy of the predissociation limits. From that it follows that at the upper predissociation limit (11.054 volts) a dissociation into  $^3P + ^1S$  takes place, i.e., that  $D(\text{CO})$  is 6.886 volts (cf. table 1). The closeness of the agreement between the difference of the predissociation limits and the difference of the excitation energies makes this value of  $D(\text{CO})$  rather persuasive. But a similarly close fit was found by Brons for what he thought to be a predissociation at 9.66 volts, which later on was found to be only a perturbation.

(2). If the predissociation observed by Gerö is an accidental predissociation, and the fact that the drop of intensity occurs only for a few lines is strongly in favor of this assumption, then of course the only thing that can be said about the corresponding dissociation limit is that it must be lower than 9.558 volts. Consequently, the values  $D(\text{CO}) = 11.054$  and 9.797 volts are excluded, whereas the remaining five values, 9.097 to 6.738, are all compatible with the predissociation at 9.558 volts. However, the two lowest values, 6.886 and 6.738, may be discarded here because assumption 2 is only needed instead of assumption 1 if as low a value for  $D(\text{CO})$  is considered impossible from other considerations. Thus under assumption 2, we have the three possibilities  $D(\text{CO}) = 9.097$  or 8.384 or 7.840 volts.

(3). If the drop in intensity observed by Gerö is due to ordinary perturbations, there would of course not be any predissociation at 9.558 volts and therefore all the seven possibilities for  $D(\text{CO})$  previously mentioned, from 11.054 to 6.738 (cf. table 1), would still have to be considered. But assumption 3 will only be made if for some other reason values of  $D(\text{CO}) \leq 9.558$  volts are excluded, so that this assumption really means that  $D(\text{CO})$  is either 11.054 or 9.797 volts.

Thus only assumption 1 leads to a single unambiguous value for  $D(\text{CO})$ , namely, the very low value 6.886, whereas assumption 2 gives the three possibilities 9.097, 8.384, and 7.841 volts, and assumption 3 gives the two values 11.054 or 9.797 volts. To the author assumption 2 seems the most probable.

A Birge-Sponer extrapolation of the vibrational levels of the ground state and the  $A^1\Pi$  state, for which a long series of vibrational levels is observed, does not lead to any definitive decision if account is taken of the uncertainty in these extrapolations. One may, perhaps, say that they seem rather incompatible with as low a value for  $D(\text{CO})$  as 6.886 or 7.841 volts and also with as high a value as 11.054 volts.<sup>18</sup>

<sup>18</sup> Birge and Hopfield (3) have found an apparent very rapid convergence of vibrational levels in the  $F^1\Pi$  state, at about  $104,500 \text{ cm}^{-1}$ . This is difficult to reconcile

So far we have only discussed purely spectroscopic data, and we have seen that on the basis of these a completely unambiguous value for  $D(\text{CO})$  cannot be given as yet. But at any rate it has been established that the true value for  $D(\text{CO})$  must be one of the seven values given in the table. Of these from purely spectroscopic reasons 9.097 and 8.384 volts seem to be the most probable. Since these two values correspond to predissociation of the  $B^1\Sigma$  state into  $^3P + ^1D$  and  $^1S + ^3P$ , respectively, it follows from the Wigner-Witmer rules that the selection rule  $\Delta S = 0$  is violated in the predissociation (singlet-triplet intercombination). This, however, is not an argument<sup>17</sup> against these values, because the predissociation is weak, as mentioned above, and intercombinations are known to occur in carbon monoxide, though very weakly.

### III. HEAT OF SUBLIMATION OF CARBON AND DISSOCIATION ENERGY OF THE CN RADICAL

One may try to come to an unambiguous value for  $D(\text{CO})$  by using some non-spectroscopic data which, though perhaps not very accurate themselves, yet might help to decide between the possible  $D(\text{CO})$  values enumerated above. By well-known thermochemical relations the value of  $D(\text{CO})$  is closely connected with the value  $L_1$  for the heat of sublimation of carbon and also with the heat of dissociation of the CN molecule.

From the equations:

$$\begin{aligned} C_{gr.} + \frac{1}{2}O_2 &= CO + 27.40 (\pm 0.12) \text{ kg-cal.}^{18} \\ O(^3P) &= \frac{1}{2}(O_2) + 58.2 (\pm 0.4) \text{ kg-cal.} \\ C(^3P) &= C_{gr.} + L_1 \\ CO &= C(^3P) + O(^3P) - D(\text{CO}) \end{aligned}$$

it follows that

$$L_1 = D(\text{CO}) - 85.6 (\pm 0.5) \text{ kg-cal.}$$

It has to be noted that here  $L_1$  means the heat of sublimation of graphite at 0°K. into normal carbon atoms in the  $^3P$  state, because  $D(\text{CO})$  refers to dissociation into normal atoms from its lowest state.

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with any of the  $D(\text{CO})$  values discussed here. But, as pointed out in a private letter of Prof. Birge to the author, their data are not sufficient to establish definitely this convergence limit.

<sup>17</sup> This argument is used by Asundi and Samuel (1).

<sup>18</sup> Private communication from F. D. Rossini.

From the equations:

$$\begin{aligned}
 \text{CN} &= \text{C}^3\text{P} + \text{N}^4\text{S} - D(\text{CN}) \\
 \frac{1}{2}(\text{CN})_2 &= \text{CN} - 38.5 (\pm 2) \text{ kg-cal.} \quad (13) \\
 \text{C}^3\text{P} + \text{O}^3\text{P} &= \text{CO} + D(\text{CO}) \\
 \text{N}^4\text{S} &= \frac{1}{2}(\text{N}_2) + 84.7 (\pm 0.1) \text{ kg-cal.} \\
 \frac{1}{2}\text{O}_2 &= \text{O}^3\text{P} - 58.2 (\pm 0.4) \text{ kg-cal.} \\
 \text{CO}_2 + \frac{1}{2}\text{N}_2 &= \frac{1}{2}(\text{CN})_2 + \text{O}_2 - 128.2 (\pm 2.5) \text{ kg-cal.}^{19} \\
 \text{CO} + \frac{1}{2}\text{O}_2 &= \text{CO}_2 + 66.76 (\pm 0.03) \text{ kg-cal.}^{18}
 \end{aligned}$$

we obtain:

$$D(\text{CN}) = D(\text{CO}) - 73.4 (\pm 4) \text{ kg-cal.}$$

The values for  $L_1$  and  $D(\text{CN})$  which thus result from the various  $D(\text{CO})$  values are given in the last three columns of table 1.

No definite conclusions can be drawn from the  $D(\text{CN})$  values, because a direct determination of  $D(\text{CN})$  has so far only been possible by Birge-Sponer extrapolations. These extrapolations do not agree with  $D(\text{CN})$  values below about 6 volts, so that from this point of view the  $D(\text{CO})$  values 11.054, 9.797, and 9.098 seem most probable.

The calculated values for  $L_1$  range from 169 to 70 kg-cal. per mole. Until recently a value of about 150 kg-cal. derived by Kohn and Guckel was generally accepted. This would be compatible only with the  $D(\text{CO})$  value 9.797 volts = 225.8 kg-cal. Now Marshall and Norton (27) propose a value  $L = 178$  kg-cal., which as seen from table 1 would be only compatible with  $D(\text{CO}) = 11.054$  volts. These two values 9.997 and 11.054, however, are according to the previous discussion very improbable from spectroscopic reasons, though they cannot be definitely excluded. They would only be possible if it were assumed that the predissociation at 9.558 volts found by Schmid and Gerö was in reality no predissociation.

The heat of sublimation of carbon,  $L$ , as determined by thermal methods corresponds to a sublimation into a mixture of atoms and diatomic molecules, whereas the value obtained from  $D(\text{CO})$  corresponds to a sublimation into atoms only ( $L_1$ ). The correction which has to be applied to the empirical value in order to get  $L_1$  depends on  $D(\text{C}_2)$ , for which so far there is no reliable value. From the calculation of Vaughan and Kistiakowsky (38) it seems, however, impossible that this correction could bring Marshall and Norton's value down to 125 kg-cal. or even 75 kg-cal., as would be necessary if  $D(\text{CO}) = 9.097$  or 6.886 volts, respectively.

Schmid and Gerö (36a), in order to explain the discrepancy between their value  $D(\text{CO}) = 6.886$  volts and the experimental  $L$  value, have suggested

<sup>19</sup> This is the average of the two rather diverging values given by K. v. Wartenberg and K. Schütza (39) and J. McMorris and R. M. Badger (28).

the following explanation. The products of the sublimation are not normal carbon atoms in the  $^3P$  state, but excited carbon atoms in the tetravalent  $^4S$  state. As the excitation energy of this state is 4.32 volts = 99 kg-cal., it would just explain the difference between the experimental  $L = 178$  kg-cal. and the  $L_1$  value calculated from  $D(\text{CO}) = 6.886$  for sublimation into normal atoms:  $L_1 = 73$  kg-cal. In equilibrium, of course, all atoms, even if they have left the solid carbon in the  $^4S$  state, would return to the  $^3P$  ground state and thereby give their energy back to the system, so that in equilibrium the low value  $L_1 = 73$  kg-cal. ought to be measured. But in the experiments of Marshall and Norton the vapor pressure of carbon is determined not by equilibrium measurements but by the loss in weight of a piece of graphite in a vacuum at high temperatures. Thus once a carbon atom in the  $^4S$  state has left the graphite its excess energy over  $^3P$  will not be given back to the graphite, i.e., one has really to supply each carbon atom with the energy which is necessary to evaporate it in the  $^4S$  state. The value measured by Marshall and Norton would, according to this interpretation, be a sort of activation energy for evaporation of carbon, not the net sublimation energy.

A somewhat similar situation has very recently been found by Melville and Gray (29) for red phosphorus. The static vapor pressure is found to be about  $10^7$  times larger than the vapor pressure derived from the loss of weight of the solid in a vacuum. This is due to the fact that, as was shown by separate experiments, only  $P_2$  molecules evaporate from and condense on solid red phosphorus, whereas, in equilibrium the vapor consists mostly of  $P_4$  molecules, which of course have much lower energy than  $P_2$  molecules. In equilibrium measurements it is the net energy difference,  $P_4 - \text{solid}$ , which matters, whereas for the dynamic method, it is the energy difference  $P_2 - \text{solid}$ . As the latter is much larger than the former, the anomalously low rate of evaporation results.

Though the assumption that carbon in the solid state (graphite, diamond) is in the  $^4S$  tetravalent state seems very probable, according to modern theories of valence, it is, however, not at all necessary to assume that immediately after evaporation a carbon atom is still in the  $^4S$  state.

As a first approximation we may expect on the basis of current valence theories that a  $^4S$  carbon atom is strongly attracted, whereas a  $^3P$  carbon atom is repulsed by solid carbon, so that we obtain the potential curves of figure 8, which intersect each other. In higher approximation, however, according to the Wigner-v. Neumann theorem of non-crossing of potential curves, the potential curves will follow the dotted lines which do not intersect. Thus in separating an atom from solid carbon it goes over into the normal  $^3P$  state, but only across a maximum of potential energy ("potential hill") which is higher than the asymptote. Nothing, so far, can be



said about the height of the potential hill. It might even be zero if a  $^3P$  atom instead of being repulsed is slightly attracted by solid carbon.

At any rate, these considerations show the following: (1) It is very improbable that if solid carbon is built up of  $^3S$  atoms the full excitation energy of the  $^3S$  state has to be supplied in excess of the net sublimation energy ( $L_1$ ) in order to evaporate carbon in a vacuum. This means at the same time that Schmid and Gerö's low value, 6.886 volts, for  $D(CO)$  is very improbable. (2) It seems possible that the heat of sublimation of carbon measured in Marshall and Norton's way is larger than the net heat of sublimation in consequence of the potential hill. This opens a possibility that the heat of sublimation measured by Marshall and Norton is yet compatible with  $D(CO)$  values lower than 11.06 volts.

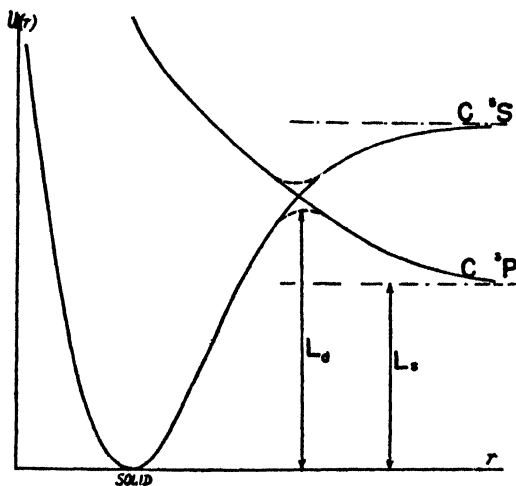


FIG. 8. Potential curves for sublimation of carbon

The two values for  $D(CO)$ , 9.097 and 8.385 volts, which resulted as the most probable ones from a discussion of the purely spectroscopic data, are thus not necessarily in contradiction to the thermal data on  $L$ .<sup>20</sup> As it seems reasonable to assume the potential hill for evaporation of carbon as small as possible, the larger of the two  $D(CO)$  values given seems the more probable. Thus we have as the most probable values:<sup>21</sup>

<sup>20</sup> In the discussion following the paper at Pittsburgh it was pointed out by Dr. Dushman that the length of life of carbon filament lamps indicates that the vapor pressure is low and the heat of sublimation correspondingly high. But here again we have a dynamic method, which on the basis of the above argument should give too high a value for  $L$ .

<sup>21</sup> Essentially the same values were also considered as most probable by Goldfinger, Lasareff, and Rosen (14) and Herzberg (19a). But they did not yet know the new data of Schmid and Gerö on the predissociation at 9.57 volts.

$$D(\text{CO}) = 9.097 (\pm 0.005) \text{ volts} = 209.7 (\pm 0.1) \text{ kg-cal.}^{22}$$

$$L_1 = 124.1 (\pm 0.5) \text{ kg-cal.}$$

$$D(\text{CN}) = 5.9 (\pm 0.2) \text{ volts} = 136 (\pm 4) \text{ kg-cal.}$$

But it has to be stressed that these values, though very probable, are not yet definitely established.

In concluding, a few ways may be mentioned which could lead to a definite decision.

A further investigation of the spectrum of the carbon monoxide molecule will be important in this connection, because it might result in the discovery of new predissociation limits and perhaps some which allow more definite conclusions to be drawn than the ones known so far.

Similarly, a further investigation of the spectrum of CN might result in a reliable determination of the dissociation energy of this molecule from which, according to the above,  $D(\text{CO})$  can be obtained.

Furthermore, if it were possible to show definitely that the drop in intensity observed by Gerö in the fourth positive group of carbon monoxide is due to accidental predissociation or ordinary predissociation, it would mean that 9.57 volts is definitely an upper limit for  $D(\text{CO})$ , which in the above could only be assumed as very probable. This could comparatively easily be accomplished by investigating the fourth positive group of carbon monoxide in absorption with high dispersion. If there is no intensity anomaly in the 9-0 band at about 1300 A.U. in absorption, it means that the intensity drop observed in emission is really caused by predissociation.

A definite decision would also be possible if the question of the heat of sublimation of carbon could be unambiguously decided. In order to do that, a repetition of the early experiments of Kohn and Guckel, with modern methods, would be of great value, because it would supply an equilibrium value for  $L$ , from which a definite value for  $D(\text{CO})$  can be obtained. In addition, the measurements of the equilibrium  $L$  could decide whether the proposed explanation for the high  $L$  value of the dynamic measurements of Marshall and Norton is correct. This of course could also be accomplished if the value of  $D(\text{CO})$  and therewith of  $L_1$  could be definitely established by spectroscopic means. Apart from its importance for the exact value of  $D(\text{CO})$ ,  $L$ , and  $D(\text{CN})$ , the question of this potential hill for evaporation of carbon seems to have considerable interest in itself.

For an exact evaluation of the thermal equilibrium measurements a knowledge of the dissociation energy of  $\text{C}_2$  is necessary; this might be expected from a further investigation of the  $\text{C}_2$  spectrum.

In a recent paper which was received after the manuscript of this paper

<sup>22</sup> The limits of error given do not include the possible error of the conversion factors.

was completed Goldfinger and Jeunehomme<sup>23</sup> have calculated the vapor pressure curves of carbon for the three values  $L_1 = 168.8$ ,  $123.6$ , and  $107.2$  kg-cal., corresponding to the  $D(\text{CO})$  values  $11.06$ ,  $9.10$ , and  $8.39$  volts. The empirical vapor pressures, except the data obtained by the dynamical method, all lie between the curves for  $L_1 = 168.8$  and  $123.6$  kg-cal. For  $L_1 = 107.2$  kg-cal. the equilibrium vapor pressure would reach 1 atm. already at  $2500^\circ\text{K}$ ., which seems to contradict all experiments with carbon at such temperatures. The vapor pressures for  $L_1 = 107.2$  kg-cal. are by several powers of 10 higher than any of those observed. Goldfinger and Jeunehomme therefore conclude that  $L_1 = 123.6$  and correspondingly  $D(\text{CO}) = 9.08$  volts are the most probable values for these quantities, i.e., essentially the same values as those proposed here.

#### SUMMARY

The various spectroscopic methods for the determination of dissociation energies  $D$  of diatomic molecules are briefly summarized. The conditions under which the  $D$  values obtained spectroscopically are dependable are treated in detail. On the basis of this discussion the various discordant values for  $D(\text{CO})$  recently proposed by a number of investigators are dealt with. None of these values is without doubt. This must also be said about the heat of sublimation  $L$  of carbon and about  $D(\text{CN})$  which may be obtained from  $D(\text{CO})$  and well-known thermochemical data. However, a number of reasons are given which lead to  $D(\text{CO}) = 9.097 (\pm 0.005)$  volts =  $209.7 (\pm 1)$  kg-cal.,  $L_1 = 124$  kg-cal.,  $D(\text{CN}) = 5.9 (\pm 0.2)$  volts =  $136 (\pm 4)$  kg-cal. as the most probable values. One of the points is that the predissociation of carbon monoxide recently found by Schmid and Gerö probably is a case of accidental predissociation. This eliminates the necessity of assuming as low a value for  $D(\text{CO})$  as Schmid and Gerö have derived. The discrepancy between the value of  $L_1$  given here and that recently obtained by Marshall and Norton from a measurement of the evaporation of carbon *in vacuo* is tentatively explained by the assumption of a potential hill which the individual atoms have to surmount in order to come from the solid to the evaporated state and *vice versa*. Investigations by which this question and the question of the values of  $D(\text{CO})$ ,  $L$ , and  $D(\text{CN})$  may be definitely settled are outlined.

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<sup>23</sup> The writer is indebted to Dr. Goldfinger for sending him an advance copy of this paper, which is now in press.

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*Note added in proof:* At the Princeton Symposium on Molecular Structure (December 31, 1936 to January 2, 1937) the question of the possibility of a potential hill for the evaporation of carbon was further discussed by K. F. Herzfeld, E. Teller, and the author. According to an idea of Teller a potential hill for the evaporation of graphite will arise owing to the fact that in the process of evaporation for every alternate carbon atom two C—C bonds have to be broken instead of the average  $3/2$  bonds, that is, on this assumption the dynamic heat of sublimation should be 33 per cent higher than the equilibrium value. This is, at least roughly, in agreement with the observed values if the equilibrium value for  $L$  given above is accepted. This agreement forms another argument in favor of the values for  $D(\text{CO})$ ,  $L$ , and  $D(\text{CN})$  proposed here.



## QUANTITATIVE LYOTROPY<sup>1</sup>

ANDR. VOET<sup>2</sup>

*University of Amsterdam, Amsterdam, Netherlands*

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Until recently the lyotropic activity of different ions has been expressed only qualitatively. A quantitative investigation of the lyotropic series has now given a deeper insight into the mechanism of ionic action.

It has been shown (7, 8) that, on salting out lyophilic colloids with mixtures of sodium sulfate and other sodium salts, the amounts of both salts that are necessary to bring about flocculation are in linear relationship. Except at very low concentrations, the salt action is perfectly additive. Figures 1 and 2 show this behavior for agar and gelatin. It is remarkable that several ions counteract the salting-out action of the sulfate ion; this "salting-in" effect does not depend on the ion only, but also on the nature of the colloid. It appears that a proper measure for the salting-out action of the ions is expressed by the angle between the lines in the diagram and the axis of the abscissae. If  $\alpha$  be this angle for a certain salt in the case of gelatin and  $\beta$  of the same salt in the case of agar, the following relation holds:

$$\cot \alpha = A \cot \beta + B$$

The directions of the lines in both diagrams are in projective relationship to each other, as has been pointed out by Bruins (3). Ascribing to every ion a number,  $N$ , fixed by the following relation:

$$N = a \cot \varphi + b$$

where  $a$  and  $b$  are constants and  $\varphi$  is the angle formed by the salt-line of the ion and the axis of the abscissae in the diagram, the angles are different in the case of different colloids, but the number  $N$  is characteristic for every ion. Fixing a scale, we use two arbitrary numbers. Choosing  $\text{SO}_4^{--} = 2.00$  and  $\text{Cl}^- = 10.00$ , we find from the diagram:

$$\begin{aligned} N &= 4.00 \cot \varphi + 10.00 \text{ (agar)} \\ N &= -4.78 \cot \varphi + 11.15 \text{ (gelatin)} \end{aligned}$$

<sup>1</sup> Presented at the Ninety-second Meeting of the American Chemical Society, held in Pittsburgh, Pennsylvania, September, 1956.

<sup>2</sup> Research Fellow of the Netherlands-America Foundation.

The calculated  $N$  values are in good agreement (see table 1). Computations give for the other ions the numbers shown in table 2.

This method enables us to predict the salting-out action of different salts in the case of other colloids, provided that the action of two ions is known. This has been proved by experiments carried out on hemoglobin (5). According to this view a linear relationship between the flocculating action

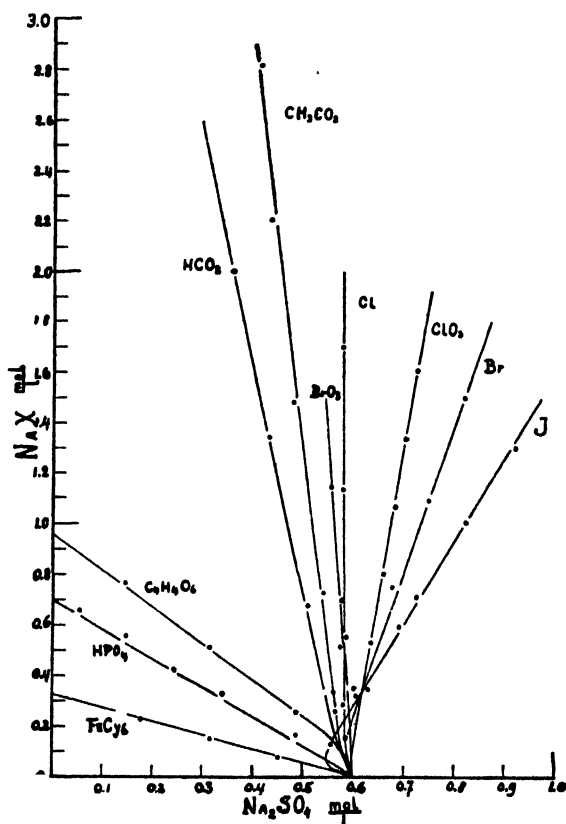


FIG. 1. Concentrations of different sodium salts plotted against concentrations of sodium sulfate, mixtures of which are necessary to bring about flocculation of agar-agar sols.

of the different sodium salts and the lyotropic numbers  $N$  is required (figure 3).

It can be shown that the numbers obtained in the case of salting-out experiments with lyophilic colloids play an important part in other lyotropic phenomena.

*a. Swelling.* Plotting the relative increase in weight of gelatin, swollen

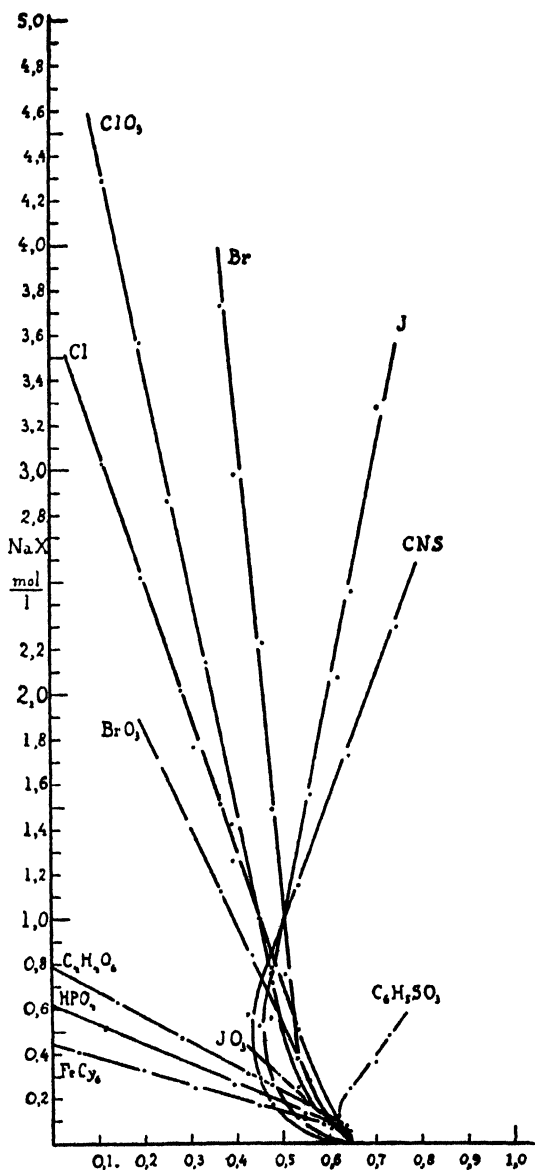


FIG. 2. Concentrations of different sodium salts plotted against concentrations of sodium sulfate, mixtures of which are necessary to bring about flocculation of gelatin sols.



in different solutions of sodium salts of the same concentration against the lyotropic numbers of the respective anions, linear relations occur (9). This is shown in figures 4a and 4b for temperatures of 0°C. and 18°C. Both lines cut the axis at the point  $N = 9.8$ , this number indicating the

TABLE 1  
*Calculated values of  $N$*

	$\text{BrO}_3^-$	$\text{NO}_3^-$	$\text{ClO}_3^-$	$\text{Br}^-$	$\text{I}^-$
Agar .....	9.72	10.1	10.74	11.50	12.50
Gelatin .....	9.38	10.2	10.58	11.14	12.48
Number used .....	9.55	10.1	10.65	11.30	12.50

TABLE 2  
*Calculated values of  $N$  for other ions*

Ion .....	$\text{F}^-$	$\text{IO}_3^-$	$\text{H}_2\text{PO}_4^-$	$\text{NO}_2^-$	$\text{ClO}_4^-$	$\text{CNS}^-$
Value of $N$ .....	4.8	6.25	8.2	11.6	11.8	13.25

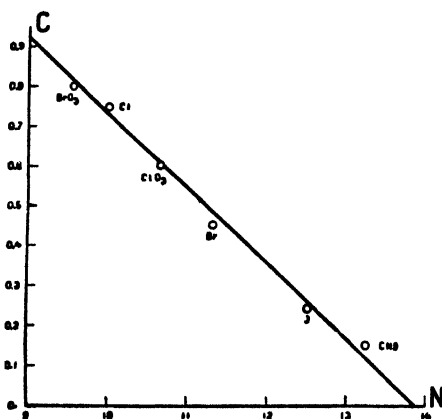


FIG. 3. Concentrations of different sodium salts, necessary to flocculate hemoglobin sols, plotted against the lyotropic numbers.

difference between ions which increase and those which decrease the swelling of gelatin.

*b. Gelation and solution of lyophilic colloids.* If Pascheles' data about gelation and solution temperatures of gelatin in salt solutions are plotted against the lyotropic numbers of the respective ions for various salt concentrations, linear relations occur (15, 6) (see figure 5).

*c. Rate of saponification of esters.* Hoeber's data on the rate of saponification of esters (10) as influenced by different salts, as well as Arrhenius' data (1), form straight lines, when plotted against lyotropic numbers (9) (see figure 6).

*d. Viscosity of salt solutions.* The viscosities of different salt solutions, if taken in the same valency group are, as has been pointed out by Merkel, in linear relationship with the lyotropic numbers, shown in figure 7 for

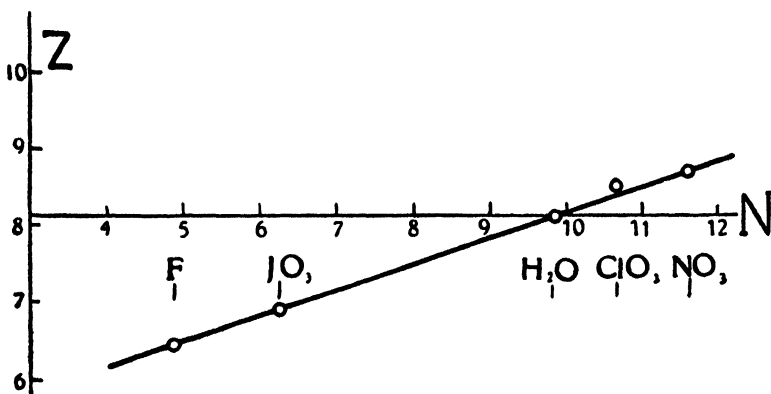


FIG. 4a. Relative weight increase of gelatin, swollen at 0°C., in different solutions of sodium salts of the same concentration, plotted against the lyotropic numbers.

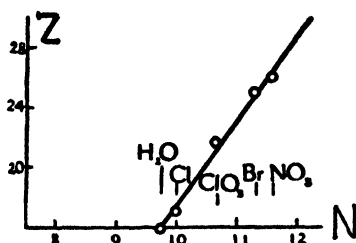


FIG. 4b. Relative weight increase of gelatin, swollen at 18°C. in different solutions of sodium salts of the same concentration, plotted against the lyotropic numbers.

different univalent sodium salts (12). This enables us to calculate the viscosity of salt solutions up to normal concentrations, within a few tenths of a per cent, when only two in the group are known.

The lyotropic numbers of the alkaline earth ions may easily be computed from their viscosity (12). Analogous regularities occur equally for this group as for the alkaline and halide ions.

The lyotropic numbers of cations have been calculated from the flocculating action of different salts on gold sols (9, 19). It appeared that only

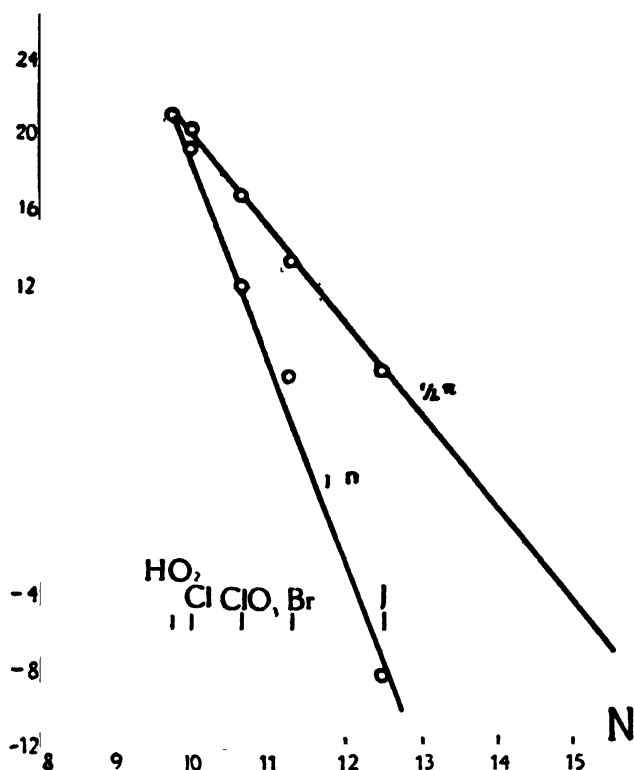


FIG. 5. Gelation temperature of gelatin in different solutions of sodium salts, plotted against the lyotropic numbers.

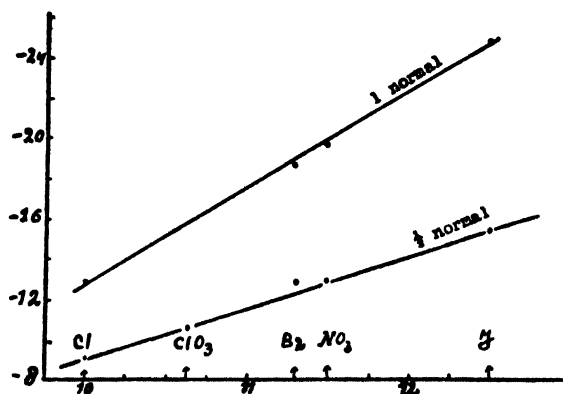


FIG. 6. Rate of saponification of ethyl acetate as influenced by different solutions of sodium salts, plotted against the lyotropic numbers.

those experiments could be used in which the decrease in the number of particles had been counted during the flocculation. From projective

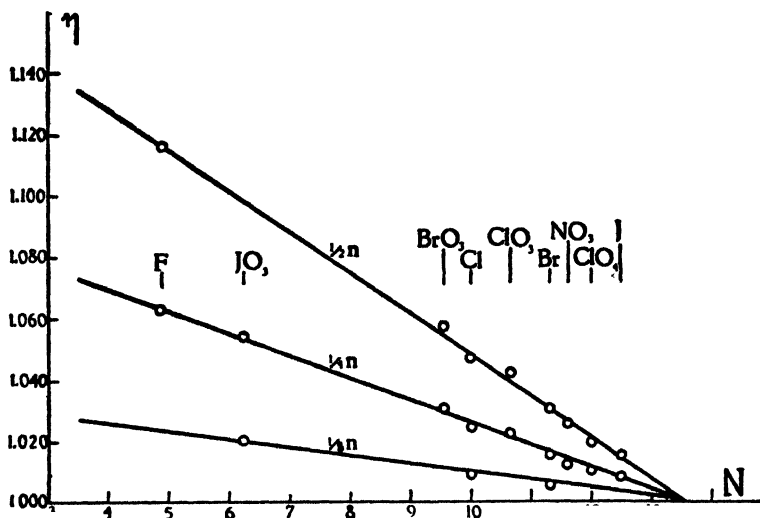


Fig. 7. Viscosity of different solutions of sodium salts with monovalent anions, plotted against the lyotropic numbers.

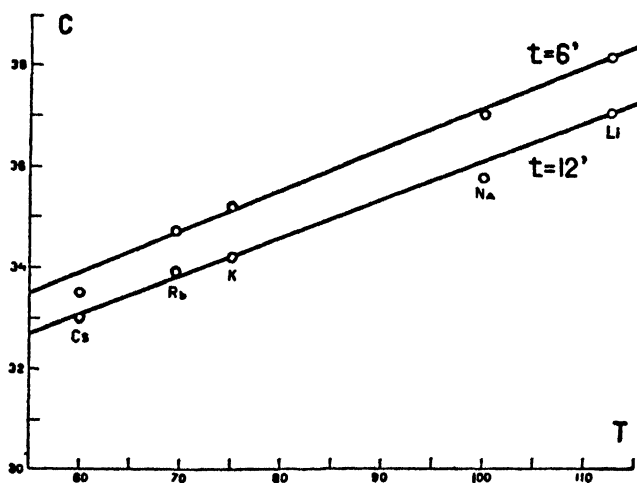


Fig. 8. Concentrations of different alkaline chlorides, causing the same decrease in the number of particles of a gold sol in the same time interval, plotted against the lyotropic numbers.

relations between the time-flocculation curves in the diagram, the numbers in table 3 for the alkaline series were derived from Tuorila's flocculation

data (16). In table 3 the numbers for sodium and potassium are arbitrary, to fix the scale. It can be shown that these numbers are in linear relationship with various flocculation data. Figures 8 and 9 show this relation in the case of flocculation of gold and paraffin sols.

As with anions, these cation numbers are important in different lyotropic experiments. Linear relations are found in several data about electro-

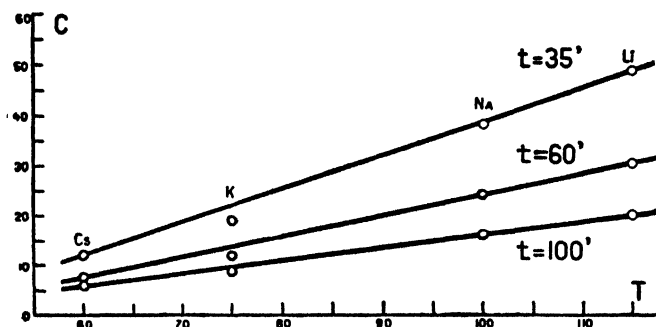


FIG. 9. Concentrations of different alkaline chlorides, causing the same decrease in the number of particles of a paraffin sol in the same time interval, plotted against the lyotropic numbers.

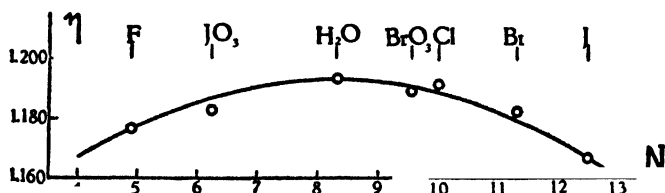


FIG. 10. Viscosity of dextrin in different solutions of sodium salts, plotted against the lyotropic numbers.

TABLE 3  
*Lyotropic numbers of cations of the alkaline series*

Cation . . . . .	Li <sup>+</sup>	Na <sup>+</sup>	K <sup>+</sup>	Rb <sup>+</sup>	Cs <sup>+</sup>
<i>T</i> .....	115	100	75	69.5	60

kinetic potentials. The ionic exchange in artificial permutites (11) follows the same laws.

If the influence of the ions is more complicated, we cannot expect linear relationships. In the case of the viscosity of dextrin dissolved in different salt solutions, a curve was obtained when the data were plotted against the lyotropic numbers (figure 10). The adsorption of electrolytes by starch

is still more complicated. Plotting the adsorption data of an experiment on *amylum solani* against the lyotropic numbers, a cubic curve was obtained (13) (see figure 11). The usefulness of the quantitative method is clearly

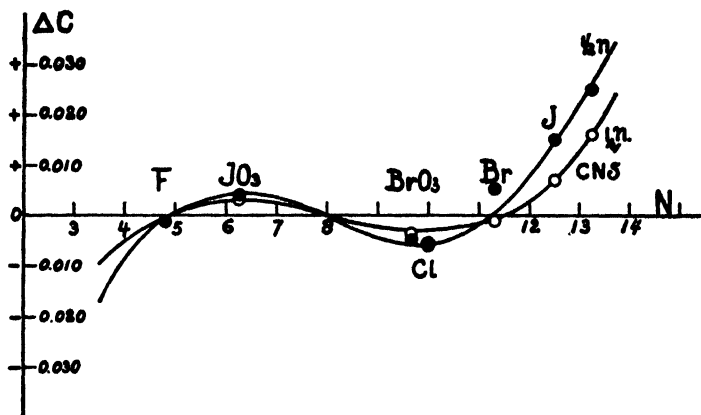


FIG. 11. Adsorption of sodium salts by potato starch, plotted against the lyotropic numbers.

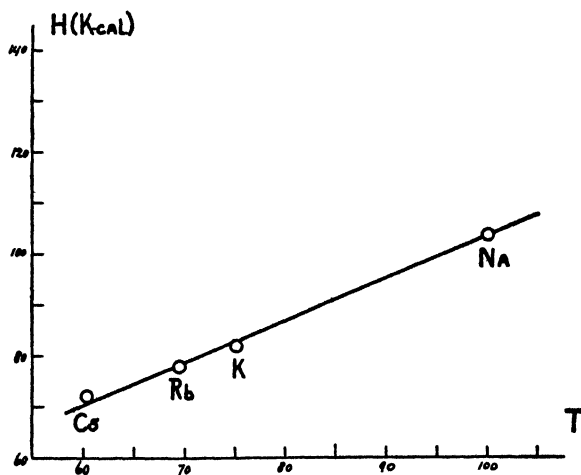


FIG. 12. Heat of hydration of alkaline ions, plotted against the lyotropic numbers

shown in these cases. According to older views, the lyotropic effect would be in complete disorder.

It has been shown that the surface tension of molten salts (14) at 1000°C. is in linear relationship with the lyotropic numbers. This proves clearly that the numbers are independent of the temperature.

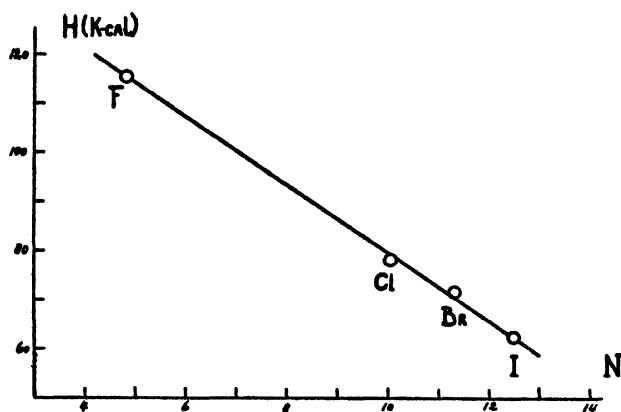


FIG. 13. Heat of hydration of halide ions, plotted against the lyotropic numbers

TABLE 4  
Heat of hydration of ions

Ion.....	$\text{IO}_3^-$	$\text{H}_2\text{PO}_4^-$	$\text{BrO}_3^-$	$\text{NO}_2^-$	$\text{ClO}_3^-$	$\text{NO}_3^-$	$\text{ClO}_4^-$	$\text{CNS}^-$
$H$ (in kg-cal.) .....	114	98	89	82	79	71	70	58

Standard values:  $\text{Cl}^- = 85$ ;  $\text{I}^- = 64$  kg-cal.

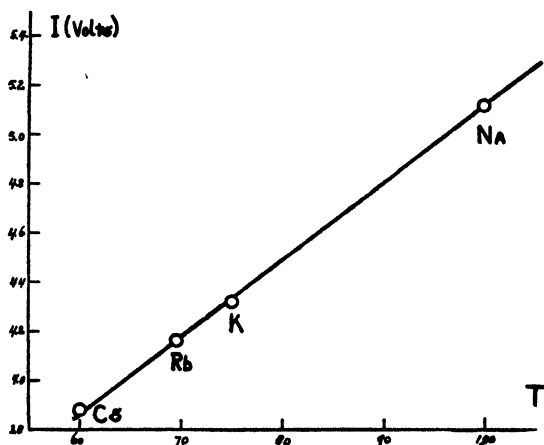


FIG. 14. Potential of ionization of alkaline metals, plotted against the lyotropic numbers.

The meaning of the lyotropic numbers can be understood from the following considerations: Plotting the lyotropic numbers against the heat of hydration of the ions, recalculated according to Fajans' method (17), linear relations are obtained (9) (figures 12 and 13). This leads to a calculation of the heat of hydration of complicated ions, the value of which was hitherto unknown (4) (see table 4). It is now clear that we could in any case have plotted heats of hydration instead of lyotropic numbers against lyotropic effects. As the former are not known in the case of every ion, we preferred to use the lyotropic numbers as a standard.

Since the heat of hydration of ions depends on the electric field which surrounds them, the lyotropic effects are beyond doubt caused by the different electric field strengths of the ions (18). This view is supported by the data on the energy of ionization, which are in perfect linear relationship with the lyotropic numbers (figure 14). A theory dealing only with the influence of ions on the state of polymerization of the  $H_2O$  molecules (2) is incorrect, since lyotropic effects occur equally in non-aqueous surroundings.

#### SUMMARY

1. The lyotropic activity of ions, influencing different phenomena, such as salting out, swelling, gelation and solation of lyophilic colloids, viscosity of salt solutions, rate of reactions, flocculation of lyophobic colloids, ionic exchange, heats of hydration, etc., are expressed quantitatively.
2. The lyotropic series are caused by different ionic field strengths.

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# ENERGY CHANGES INVOLVED IN THE ADDITION REACTIONS OF UNSATURATED HYDROCARBONS

J. B. CONANT AND G. B. KISTIAKOWSKY

*Department of Chemistry, Harvard University, Cambridge, Massachusetts*

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This paper is in the nature of a progress report. It is an attempt to survey from the point of view of the organic chemist the data which have recently been obtained in the course of a series of thermochemical studies in the Harvard laboratories (3). The aim of these studies is to measure directly the heat changes involved in chemical reactions, in particular addition reactions of all manner of unsaturated and cyclic compounds. It is usually possible to obtain much more accurate data by such direct measurements than by calculating the heat effect of an addition reaction from heats of combustion. This is particularly true, of course, in the case of compounds containing a considerable number of carbon atoms whose heat of combustion is large and where in calculating the heat of addition of two hydrogen atoms, for example, one must take the difference of two large numbers. Although the program outlined is in its first stages, a number of interesting results have already been obtained which seem to throw considerable light on a number of problems of the organic chemist. For this reason, it seems worth while to present this summary of the work, incomplete as it is, and to point out some of the questions which await solution.

In table 1 are collected all the data which have been obtained thus far in the direct determination of the heats of hydrogenation. These measurements are all made for gas-phase reactions. For the experimental details in regard to the adiabatic calorimeter used, the method of measurement, and the purification of the compounds, the reader may consult the original papers. In general the accuracy of the data is of the order of 0.1 to 0.3 per cent. The table is divided into sections according to the number of hydrogen atoms involved in the addition reaction whose heat was measured.

Considering, first, section A of table 1 it is evident that the substitution of the hydrogen atoms of ethylene by alkyl groups diminishes the heat evolved in the hydrogenation. This effect reaches its maximum in the compounds measured in the case of tetramethylethylene with which 6.2

Cal. less heat is evolved in hydrogenation than in the case of the parent hydrocarbon. However, the effect of progressively substituting the four hydrogen atoms by methyl groups is not additive, but on the contrary each subsequent alkyl group is less effective than the preceding one. The

TABLE 1

*Heats of hydrogenation of unsaturated and aromatic compounds at 82°C. (355°K.) (ΔH) in large calories*

COMPOUND	ΔH	COMPOUND	ΔH
A. Addition of H <sub>2</sub>			
Ethylene.....	-32.8	<i>as</i> -Methylethylethylene.....	-28.5
Propylene.....	-30.1	Pentene-2 (mixture).....	-28.0
Butene-1.....	-30.3	Cyclopentene.....	-26.9
Heptene-1.....	-30.1	Cyclohexene.....	-28.6
Isopropylethylene.....	-30.3	Trimethylethylene.....	-26.9
Tertiary-butylethylene.....	-30.3	Tetramethylethylene.....	-26.6
Neopentylethylene.....	-29.5	Vinyl acetate.....	-31.1
Isobutene.....	-28.4	Crotonaldehyde.....	-25.2
Butene-2 ( <i>trans</i> ).....	-27.6	2-Ethoxypropene.....	-25.1
Butene-2 ( <i>cis</i> ).....	-28.6	Acetone.....	-13.4
<i>as</i> -Methylisopropylethylene.....	-28.0	Methyl ethyl ketone.....	-13.2
B. Addition of 2H <sub>2</sub>			
Allene.....	-71.3	Limonene*.....	-54.1
Butadiene-1,3.....	-57.1	α-Phellandrene*.....	-53.4
2,3-Dimethylbutadiene-1,3.....	-53.9	α-Terpinene*.....	-50.7
Pentadiene-1,3.....	-54.1	Pentadiene-1,4.....	-60.8
Cyclohexadiene-1,3.....	-55.4	Hexadiene-1,5.....	-60.5
Cyclopentadiene-1,3.....	-50.9	Furane.....	-36.6
		Divinyl ether.....	-57.2
C. Addition of 3H <sub>2</sub>			
Benzene.....	-49.8	<i>o</i> -Xylene.....	-47.3
Ethylbenzene.....	-48.9	Dihydroindene.....	-45.8
Mesitylene.....	-47.6		
D. Addition of 4H <sub>2</sub>			
Styrene.....	-77.5	Indene.....	-69.9

\* Compounds of somewhat uncertain purity.

jump from ethylene to propylene, for example, is 2.7 Cal., while that from trimethylethylene to tetramethylethylene is only 0.3. A comparison of propylene, butene-1, heptene-1, tertiary-butylethylene, neopentylethylene and isopropylethylene shows that within a few tenths of a Calorie the

methyl, ethyl, *n*-amyl, isopropyl, tertiary-butyl, and neopentyl groups are equally potent in decreasing the affinity of the double bond for hydrogen. The differences between these compounds, while greater than the experimental error, are clearly second-order effects compared to the action of an alkyl group in general. The three compounds of the type  $R_2C=CH_2$ , which have been measured give the same value for  $-\Delta H$  of hydrogenation (28.2) within 0.2 Cal., and this value is almost the same as that for *cis*-butene-2 ( $CH_3CH=CHCH_3$ ) (28.6). Here again, omitting a consideration of second-order effects, two alkyl groups in the  $\alpha, \alpha$ - or  $\alpha, \beta$ -position (if *cis*) produce essentially the same effect. These generalizations seem to apply to simple primary and secondary alkyl groups and less accurately to the more highly branched ones.<sup>1</sup>

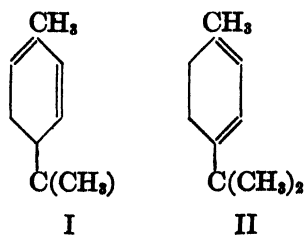
The difference of 1.0 Cal. between the *cis*- and *trans*-forms of butene-2 is striking, the *cis*-form having the greater affinity for hydrogen as measured by the total energy change. The value of cyclohexene is practically identical with that of *cis*-butene-2, as would be expected. Cyclopentene, however, is less unsaturated by 1.7 Cal.; this fact will be referred to later.

We may now consider the effect of a multiplicity of double linkages. Sections B and D of table 1 at first sight reveal a number of interesting regularities. The very large value of allene being considerably more than twice the figure for ethylene shows that this compound may be considered the most highly unsaturated compound yet examined by these methods. A comparison of the three compounds of the type  $CH_2=CH(CH_2)_n-CH=CH_2$ , in which  $n = 0, 1$ , and  $2$ , shows the effect of conjugation ( $n = 0$ ) on the value of  $-\Delta H$ , lowering it by about 3.5 Cal., an amount, it may be noted in passing, no greater than that produced by the introduction of two alkyl groups into ethylene. For many purposes of the *organic chemist*, however, it is more convenient to convert the results of sections B, C, and D of table 1 into the value of  $\Delta H$  for the addition of only one mole of hydrogen. The results are then directly comparable with each other and with those in section A of table 1. The method of calculating the value of  $\Delta H$  for the addition of the first pair of hydrogen atoms is, of course, very simple where the expected product (a substituted ethylene) has already been examined. For example, the addition of  $H_2$  to allene

<sup>1</sup> The two isomeric octenes which have been examined yielded rather surprising results which, if their purity can be relied upon, indicate divergencies from the rules for more simple hydrocarbons. 2,4,4-Trimethylpentene-1 gave a value of 27.2 as compared with 28.4 for isobutene. But since the neopentyl group by itself was more effective in lowering  $-\Delta H$  than any of the other alkyl groups tried, this discrepancy is not serious. The other compound, 2,4,4-trimethylpentene-2, with 28.4 Cal., is completely out of line.

would yield propylene and, since  $-\Delta H$  of hydrogenation for propylene is 30.1,  $-\Delta H$  for the reaction allene +  $H_2 \rightarrow$  propylene is  $71.3 - 30.1 = 41.2$ . In the cases where the first product of the stepwise hydrogenation has not been hydrogenated in this laboratory, the value of  $\Delta H$  can be estimated from general rules developed for section A of table 1. Such cases are noted by an asterisk in table 2, where the value of  $\Delta H$  for the addition of one mole of hydrogen is given for the compounds listed in sections B, C, and D of table 1.

As table 2 illustrates, the open-chain conjugated systems give different calculated values of  $\Delta H$  for the addition of one mole of hydrogen depending on the mode of addition; the greatest amount of heat is liberated if the addition is in the 1,4-position. If one takes this maximum value of  $-\Delta H$  as a measure of the unsaturation of the system, then it is clear that butadiene-1,3 has a higher affinity for hydrogen than all compounds of the type  $R_2C=CH_2$  or  $RCH=CHR$  and only about 1 Cal. less than compounds of the type  $RCH=CH_2$ . The substitution of a methyl group on the end of the chain has diminished the maximum value by 3 Cal., an effect somewhat larger than that caused by the substitution of a methyl group in ethylene (2.7). Butadiene-1,3 is, as it were, the ethylene of the conjugated series. If this is the case the disubstituted derivative  $CH_3CH=CH-CH=CHCH_3$  might be expected to differ from the parent compound by the same order of magnitude as  $RCH=CHR$  from  $CH_2=CH_2$ . If this is so, the maximum value of  $\Delta H$  for one mole of  $H_2$  for  $CH_3CH=CH-CH=CHCH_3$  would be about  $-(+29.5 - 4.5) = -25.0$  Cal.; this estimated value is not far from that for cyclohexadiene ( $-26.8$ ) but is clearly uncertain by several tenths of a Calorie. We would seem to be safe in taking the value of cyclohexadiene as typical of the terminally disubstituted butadienes. This is confirmed by the values obtained with two substituted cyclohexadienes,  $\alpha$ -phellandrene and  $\alpha$ -terpinene, although in both cases high purity can not be guaranteed.  $\alpha$ -Phellandrene is the methylisopropylcyclohexadiene (I). The calculated value of  $-\Delta H$ ,



using cyclohexadiene and the rules of aliphatic substitution, is  $55.4 - 1.8 = 53.6$ , in excellent agreement with the observed value 53.4.  $\alpha$ -Terpinene

TABLE 2

Calculated values of  $\Delta H$  (355°K.) of hydrogenation by one mole of hydrogen




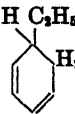
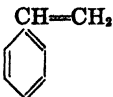
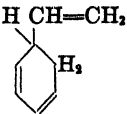
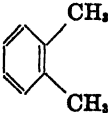
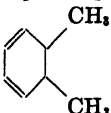
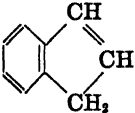
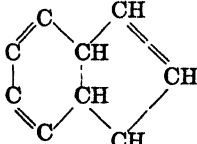
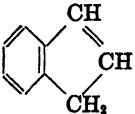
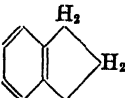
COMPOUND HYDROGENATED	MODE OF ADDITION	PRODUCT	$\Delta H$ (355°K.) 1 MOLE OF $H_2$
$CH_2=C=CH_2$		$CH_3CH=CH_2$	-41.2
$CH_2=CH-CH=CH_2$	1,4	$CH_3CH=CHCH_3$ ( <i>cis</i> )	-28.5
$CH_2=CH-CH=CH_2$	1,4	$CH_3CH=CHCH_3$ ( <i>trans</i> )	-29.5
$CH_2=CH-CH=CH_2$	1,2	$CH_3CH_2CH=CH_2$	-26.8
$CH_2=C-C=CH_2$	1,4	$(CH_3)_2C=C(CH_3)_2$	-27.3
$\begin{array}{c} CH_3 \quad CH_3 \\   \quad   \\ CH_2-C-C=CH_2 \end{array}$	1,2	$(CH_3)_2CHC=CH_2$	-25.9
$\begin{array}{c} CH_3 \quad CH_3 \\   \quad   \\ CH_2CH-CH-CH=CH_2 \end{array}$	1,4	$CH_3CH_2CH=CHCH_3$ ( <i>cis</i> )	-25.5*
$CH_3CH=CH-CH=CH_2$	1,4	$CH_3CH_2CH=CHCH_3$ ( <i>trans</i> )	-26.5*
$CH_3CH=CH-CH=CH_2$	1,2	$CH_3CH=CHCH_2CH_3$ ( <i>cis</i> )	-25.5*
$CH_3CH=CH-CH=CH_2$	1,2	$CH_3CH=CHCH_2CH_3$ ( <i>trans</i> )	-26.5*
$CH_3CH=CH-CH=CH_2$	3,4	$CH_3CH_2CH_2CH=CH_2$	-23.8*
$CH=CH-CH=CH$	1,4	$CH_3CH=CHCH_3$	-26.8
$\begin{array}{c} \text{---} CH_2-CH_2 \text{---} \\   \quad   \\ CH=CH-CH=CH \end{array}$	and 1,2	$\begin{array}{c} CH_2 \quad \quad CH_2 \\   \quad \quad   \\ CH_2CH=CHCH_2 \end{array}$	-24.0
$\begin{array}{c} \text{---} CH_2 \text{---} \\   \\ CH=CH-CH=CH \end{array}$	and 1,2	$\begin{array}{c} \text{---} CH_2 \text{---} \\   \\ CH_2-CH=CH-CH_2 \end{array}$	-8.0*
$\begin{array}{c} \text{---} O \text{---} \\   \\ CH=CH-CH=CH \end{array}$	1,4	$\begin{array}{c} \text{---} O \text{---} \\   \\ CH_2-CH=CH-CH_2 \end{array}$	(taking $\Delta H$ for this compound as for <i>cis</i> -butene-2)
$CH=CH-CH=CH$	1,2	$CH_2-CH=CH$	-11.5*
$\begin{array}{c} \text{---} O \text{---} \\   \\ CH=CH-CH=CH \end{array}$		$\begin{array}{c} CH_2 \quad \quad O \\   \quad \quad   \\ CH_2-CH=CH-CH_2 \end{array}$	(taking $\Delta H$ for this compound as for 2-ethoxypropene)
	1,4		7.4*
		(estimated twice cyclohexene)	
	1,2	Cyclohexadiene	5.6
$\begin{array}{c} C_2H_5 \\   \\ \text{---} \end{array}$	1,2 (ortho)		6.5*
$\begin{array}{c} CH_3 \\   \\ \text{---} \end{array}$	1,2 (ortho)		5.9*
$\begin{array}{c} CH_3 \quad CH_3 \\   \quad   \\ \text{---} \end{array}$	1,4		7.8*
$C_2H_5CH=CH_2$		Ethylbenzene	-28.6

TABLE 2—*Concluded*

COMPOUND HYDROGENATED	MODE OF ADDITION	PRODUCT	$\Delta H$ (355°K.) 1 MOLE OF $H_2$
		 (assuming $\Delta H = \Delta H$ of cyclohexadiene plus heptene-1)	7.9*
	1,2 (ortho) to give		8.1*
	1,2 (ortho) to give		12.4*
	to give		-24.1
Pentadiene—1,4 Hexadiene—1,5	1,2 1,2	$CH_3(CH_2)_2CH=CH_2$ $CH_3(CH_2)_3CH=CH_2$ (taking heptene-1 value in both cases)	-30.7* -30.4*

is isomeric (II) and the calculated value is  $55.4 - 2 \times 1.8 = 51.8$ , as compared with 50.7.

The introduction of two methyl groups in the 2,3-position in butadiene-1,3 is striking. Comparing the maximum figures for 1,4-addition the difference is 2.2, while the corresponding difference for the 1,2-addition is only 0.8 Cal. Again clearly, the 1,4-positions in butadiene are like the 1,2-positions in ethylene itself and the value of  $\Delta H$  is a sensitive reflection of disturbances in the molecule produced by substitution.

The value of  $\Delta H$  for one mole of hydrogen added to the unconjugated dienes is somewhat higher than the corresponding value for propylene (cf. table 1 (A) and table 2). The "exaltation" is 0.6 Cal. with the pentadiene and 0.3 Cal. with the hexadiene; this may represent the dying out with lengthening of the chain of the enormous increase evident in allene where the juxtaposition of the two double bonds has increased the affinity for hydrogen by about 11 Cal. If this is the case the affinity of butadiene

itself must be the resultant of such an increase in affinity due to the proximity of the two double linkages and what has now come to be known as the "resonance energy" of the conjugated system. From the point of view of the organic chemist it is perhaps advantageous to speak of the decreased affinity for hydrogen due to conjugation. On this basis it is clear that it is well to avoid the case of compounds with a terminal  $C=CH_2$  where a proper basis of comparison seems difficult, and consider as typical the comparison of  $RCH=CH-CH_2CH_2R$  and  $RCH=CH-CH=CHR$ . If this is done the decrease in affinity due to conjugation would appear to be in the neighborhood of 2 to 3 Cal.

When we turn to the cyclic compounds we approach the problem of so-called aromatic compounds. The unsaturation of cyclohexadiene (as measured by  $\Delta H$  of hydrogenation) is, as far as we can at present estimate, very close to that of the corresponding open-chain compound and only some 2 Cal. less than an unconjugated diene. In cyclopentadiene we have a very appreciable decrease (4.5) of affinity as compared with cyclohexadiene, whereas a comparison of cyclopentene and cyclohexene shows a decrease of affinity in the former of *ca.* 1.7 Cal. To understand these facts one should remember that cyclopentane is, according to combustion data, under a strain of some 4 Cal., while cyclohexane is not. The lower heats of hydrogenation of the five-membered rings (more positive  $\Delta H$ ) mean formally that the strain is increased by opening their double bonds. Thus cyclopentadiene must have less strain than cyclopentene, and this in turn less strain than cyclopentane. This conclusion is arrived at by supposing that no strains exist in the six-membered systems, as otherwise only a conclusion relative to the behavior of the six-membered rings is possible. In any case, however, it is in crass disagreement with the tetrahedral valence theory of carbon, which would predict increasing strain in the five-membered ring as the single bonds are replaced by the double bonds. But further facts seem to support it quite conclusively. Thus  $\Delta H$  of the 1,2 hydrogenation of dihydroindene (see table 2) is more positive (1.7 Cal.) than that of *o*-xylene and the 1,2 hydrogenation in the five-membered ring of indene is more positive than the suitably corrected heat of hydrogenation of the side chain in styrene and is actually equal to the 1,2 hydrogenation of cyclopentadiene. Reasoning again quite formally, we may say that converting the five-membered ring in indene and hydrindene to a completely saturated ring evolves less heat than would be calculated by analogy with compounds not containing a five-membered ring. It thus appears that the strain in five-membered rings increases with decreasing unsaturation. This is a most surprising result and merits further investigation.

The best method of studying this problem is by measuring the heats of



hydration of cyclic acid anhydrides and lactones; such work is now planned in this laboratory.

Recent results obtained by studying coupling reactions of hydroxy derivatives indicate a striking difference between *o*-xylene on the one hand and hydrindene on the other. Measurements of dipole moments (6) tend to confirm the evidence that there is some rather fundamental difference between these two closely related compounds. Our results are not in agreement with these findings. There is a difference of only a few Calories in heat evolved in the hydrogenation by one mole of hydrogen of these two compounds, and the difference is in the opposite direction from that predicted on the basis of "fixed bond formulae" derived from the coupling reactions.

#### CONCERNING THE CHEMICAL PROPERTIES OF AROMATIC COMPOUNDS

When we come to furane, in table 2, the decrease of  $\Delta H$  is so large (about 16 Cal.) that clearly a special factor must be involved; when we reach benzene and its derivatives the decrease is of the order of magnitude of 31 Cal. and the sign of  $\Delta H$  has become reversed. From the point of view of the chemist the value of  $\Delta F^0$  is of more practical consequence than the value of  $\Delta H$ . When  $\Delta F^0$  is equal to about  $-5$  Cal., a gaseous reaction of type  $A + B = C$  at one atmosphere pressure proceeds to a point where 1 per cent of the reactants exists at equilibrium; when  $\Delta F^0 = 3$  Cal., only 1 per cent of the product is present at equilibrium. Thus if  $\Delta F^0$  is more positive than about  $+3$ , the reaction will apparently "not proceed" under usual conditions of pressure.


The values of  $\Delta F^0$  for the addition of one mole of hydrogen at  $298^\circ\text{K}$ . for some typical unsaturated compounds are given in table 3; the values of  $\Delta H$  at  $355^\circ\text{K}$ . are taken from tables 1 and 2, reduced to  $298^\circ$ , and  $\Delta S^0$  estimated from the best data available.

An inspection of table 3 shows that although the free energy change attendant on the addition of one mole of hydrogen to many alkyl derivatives of ethylene and to butadiene and the cyclic dienes is a great deal less than for ethylene itself, the reactions will all run to practical completion. Quite different is the case of benzene; here the sign is reversed and  $\Delta F^0 = +13.6$  Cal.; the amount of product in equilibrium with the reactants is negligible. It is impossible to form cyclohexadiene from benzene directly, not because of any question of relative rates of reactions but because of the energy change involved in the addition of one mole of hydrogen to the aromatic compound. With furane a measurable equilibrium should exist if the second step could be suppressed, whereas even the small value of  $-14.8$  for cyclopentadiene is ample to ensure complete reaction with one mole of hydrogen. Towards hydrogen and a catalyst furane and

benzene are quite different in their behavior from the other unsaturated compounds; with them it is hopeless to attempt to add one pair of hydrogen atoms to the unsaturated system.

The peculiar chemical properties of benzene and its derivatives which first attracted the attention of organic chemists are clearly due to the fact that in these compounds the energy relationships are such that an addition reaction involving one double linkage (or its equivalent) will not proceed to any appreciable extent. Unfortunately, we cannot predict with any

TABLE 3  
Values of  $\Delta F^0$  for the addition of one mole of hydrogen at 298°K. for some unsaturated hydrocarbons  
(Gaseous state)

COMPOUND	ADDENDUM	PRODUCT	298°K.		
			$\Delta H$	$-T\Delta S^0$	$\Delta F^0$
$\text{CH}_2=\text{CH}_2$	$\text{H}_2$	$\text{C}_2\text{H}_6$	-32.6	8.2	-24.4
$\text{CH}_3\text{CH}=\text{CH}_2$	$\text{H}_2$	$\text{CH}_3\text{CH}_2\text{CH}_3$	-29.9	8.9	-21.0
$\text{CH}_3\text{CH}=\text{CHCH}_3$ (cis)	$\text{H}_2$	$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_3$	-28.2	8.9	-19.4
$\begin{array}{c} \text{CH}_3 \qquad \text{CH}_3 \\ \diagdown \quad \diagup \\ \text{C}=\text{C} \\ \diagup \quad \diagdown \\ \text{CH}_3 \qquad \text{CH}_3 \end{array}$	$\text{H}_2$	$(\text{CH}_3)_2\text{CHCH}(\text{CH}_3)_2$	-26.4	8.9	-17.5
$\text{C}_6\text{H}_5\text{CH}=\text{CH}_2$	$\text{H}_2$	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_3$	-28.3	8.9	-19.5
$\text{CH}_2=\text{CH}-\text{CH}=\text{CH}_2$	$\text{H}_2$	$\text{CH}_3\text{CH}=\text{CHCH}_3$ (trans)	-29.2	8.9	-20.3
$\text{CH}=\text{CH}-\text{CH}=\text{CH}$	$\text{H}_2$	$\text{CH}=\text{CH}-\text{CH}_2$	-26.5	8.8	-17.7
$\begin{array}{c} \text{CH}_2\text{CH}_2 \\   \qquad   \\ \text{CH}-\text{CH}-\text{CH}=\text{CH} \end{array}$		$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CH}_2 \\   \qquad   \qquad   \\ \text{CH}=\text{CH}-\text{CH}_2-\text{CH}_2 \end{array}$	-23.7	8.8	-14.8
$\begin{array}{c} \text{CH}_2 \\   \\ \text{CH}-\text{CH}-\text{CH}=\text{CH} \end{array}$	$\text{H}_2$	$\begin{array}{c} \text{CH}_2 \\   \qquad   \\ \text{CH}_2-\text{CH}_2-\text{CH}=\text{CH} \end{array}$	-11.4	8.9	-2.5
$\begin{array}{c} \text{O} \\   \\ \text{CH}-\text{CH}-\text{CH}=\text{CH} \end{array}$		$\begin{array}{c} \text{O} \\   \qquad   \\ \text{CH}_2-\text{CH}_2-\text{CH}=\text{CH} \end{array}$			
$\text{C}_6\text{H}_6$	$\text{H}_2$		5.8	7.8	13.6

accuracy the energy changes which accompany the interaction of unsaturated compounds with such reagents as the halogens, halogen acids, and water (with acid as a catalyst); table 4 summarizes the data now available. If one may extrapolate from these few facts it seems extremely probable that for none of the common reagents is  $\Delta F^0$  more than a few Calories more negative than for hydrogen, while for many it is much more positive. This being the case we can easily understand why benzene and its derivatives are "not unsaturated" when tested with such reagents as bromine. No addition reaction involving one mole of reagent is possible

( $\Delta F^0$  is too positive), and a simultaneous addition of two or three moles of the reagent is too difficult kinetically to occur at a measurable rate; this being the case other reactions such as substitution are possible, and proceed. Comparing styrene (phenylethylene) with propylene (table 3) we see the affinity of the former for  $H_2$  (as measured by  $\Delta F^0$ ) is 1.4 Cal. less than that of the latter; if a similar difference holds for the tetrasubstituted compounds we may predict  $\Delta F_{298}^0$  (gaseous state) for the reaction  $(C_6H_5)_2C=C(C_6H_5)_2 + H_2$  to be about  $-12.5$ . (In solution this value may be decreased or increased by as much as 2 Cal.) Tetraphenylethylene thus approaches furane, and if the energy changes with other reagents parallel those with hydrogen we should predict that this compound will not combine with iodine ( $\Delta F^0$  being 22 Cal. more positive than with  $H_2$ ) nor with hydrobromic acid ( $\Delta F^0$  perhaps 18 Cal. more positive than with  $H_2$ ) or similar reagents, among which nitric and sulfuric acids may well be included. Until more accurate data are available for simple halogenations

TABLE 4  
*Addition reactions of ethylene in the gaseous state at 298°K.*

ADDENDA (GASES)	$\Delta H$	$T\Delta S$	$\Delta F$	METHOD
	<i>Cal.</i>	<i>Cal.</i>	<i>Cal.</i>	
$H_2$	-32.6	-8.2	-24.4	Direct $\Delta H$
$Cl_2$	-42 (?)	-12 (?)	-30 (?)	Heats of combustion
$Br_2$	—	—	—	No data
$I_2$	-13.6	-11	-2.2	Direct K
$H_2O$	-10.8	-8.3	-2.5	Heats of combustion and K
$HBr$	-18 (?)	-10 (?)	-8 (?)	Heats of combustion

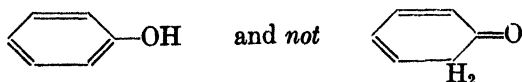
exact predictions are obviously dubious, but it is interesting to note that whereas diphenyl derivatives of ethylene combine with both chlorine and bromine, tetraphenylethylene reacts with chlorine to form a dichloride (5) but will not add bromine (1). This indicates that the free energy of addition of chlorine to a double bond is of similar magnitude to that of hydrogenation (cf. table 4) but the affinity of bromine is 10 to 15 Cal. less.

There thus emerges from a consideration of the energy changes involved in addition reactions of unsaturated compounds a clear picture of the peculiar properties of certain classes of unsaturated compounds which have been designated for generations as "aromatic." The affinity of these aromatic compounds for one mole of addendum is so small that no appreciable addition can take place quite irrespective of any considerations involving rates of reactions. This being so, other types of reactions such as substitution proceed instead of addition reactions. It is obvious, however, that there may be some compounds which will show "typical aromatic

properties" (i.e., no addition reactions involving *one* mole) when treated with certain reagents which have low affinity for the carbon-carbon double bond and yet will combine like other unsaturated compounds with other reagents. The organic chemist long ago ruled out iodine as a suitable reagent for distinguishing between aromatic and aliphatic unsaturated compounds, as it was known that this element would not combine with many simple double bonds. On the other hand, there is clear evidence that ozone will combine mole for mole even with benzene compounds. The qualitative behavior of a compound is thus clearly dependent on the reagent chosen, and if the reaction involving one mole proceeds it throws no light on whether  $\Delta F^0$  is just over the line for an essentially complete reaction or whether the free energy change is very large. The only reason for dwelling on these obvious points at such length is that in lieu of accurate quantitative data there is an almost irresistible temptation to argue from qualitative information. The much quoted cyclooctatetraene is a case in point. It is cited as being non-aromatic because it reacts with bromine, is oxidized by potassium permanganate, etc. All this might be true and yet the affinity of the compound might be essentially that of cyclohexadiene ( $\Delta F^0$  for one mole of hydrogen,  $-17.7$ ) or significantly lower by as much as 15 Cal. (if bromine and hydrogen have the same order of affinity for unsaturated compounds). Many theoretical arguments have been based on the non-aromatic nature of cyclooctatetraene. Clearly until one has quantitative data in regard to the energy changes involved when cyclooctatetraene combines with hydrogen (or some other reagent) one is on uncertain ground. The most that can be argued from the qualitative information is that its affinity for an addendum is not as low as in the case of benzene.

#### PHENOLS AND ENOLS

In addition to the chemical peculiarities of the parent hydrocarbons, aromatic compounds are also characterized by the fact that the unsaturated hydroxy compounds are stable in the enol form. Thus  $C_6H_6O$  is predominantly if not exclusively



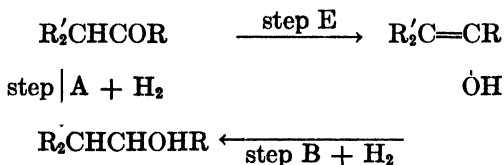
whereas  $C_2H_4O$  is  $\text{CH}_3\text{C}=\text{O}$  and not  $\text{CH}_2=\text{C}-\text{OH}$ . The relation be-

tween this property and the lowered affinity of the unsaturated system is at once apparent from the following considerations: Consider the com-

pound  $R_2'CHCOR$  and its enol  $R_2'C=CR$ , where R and R' may be of any

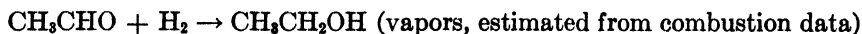


nature including parts of the same cyclic system. The reduction to  $R_2'CHCHOHR$  may proceed as follows in one of two ways:



The free energy change ( $\Delta F^0$ ) of the reduction step A is obviously equal to the sum of the free energy changes in the other two steps. Thus  $\Delta F^0$  (enolization) =  $\Delta F^0$  (reduction of carbonyl compound) -  $\Delta F^0$  (reduction of enol). The first term on the right-hand side of this equation is small (about -6) and probably only little affected by changes in structure. Therefore, as an approximation  $\Delta F^0$  (enolization) = 6 -  $\Delta F^0$  (of reduction of enol). The energy changes in the reduction of the enol will closely parallel those of the corresponding unsaturated hydrocarbon, except in cases where chelation occurs. Thus, corresponding to the low affinity of aromatic compounds for hydrogen, we find high stability of the enol (large negative values of  $\Delta F^0$  of enolization). The following rough estimates will serve as illustrations and also show how an approximate measure of the free energy of enolization of aliphatic ketones and aldehydes may be obtained.

*For acetaldehyde*



$$\Delta F_{298}^0 = -7.5 \text{ Cal.}$$



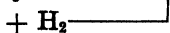
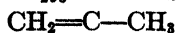
$$\Delta F_{298}^0 = -21.0 \text{ Cal. (estimated from } \Delta H_{355}^0 \text{ as mean of } -31.1 \text{ from vinyl acetate and } -28.6 \text{ from } \frac{1}{2} \text{ divinyl ether} = -30.0)^2$$

$$\Delta F_{298}^0 \text{ (enolization)} = +13.5 \text{ (wholly ketonic)}$$

*For acetone*



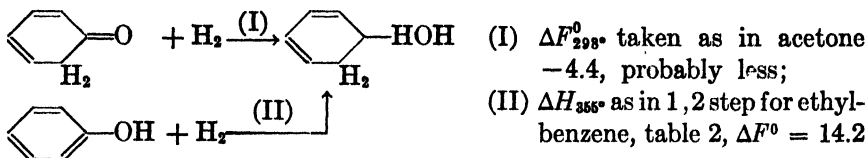
$$\Delta F_{298}^0 = -4.4$$



\* Since this paper was set in type, the heat of hydrogenation of ethyl vinyl ether has been measured and found to be -26.7 Calories. This lowers the value  $\Delta F_{298}^0$  for  $CH_2=CHOH + H_2 \rightarrow CH_3CH_2OH$  to -17.9 Calories and  $\Delta F_{298}^0$  (enolization) = +10.4 Calories.

$\Delta F_{298}^0$  (estimated from  $\Delta H_{355} = -25.1$  for 2-ethoxypropene) =  $-16.3$   
 $\Delta F_{298}^0$  (enolization) =  $+11.9$  (wholly ketonic). This value confirms the very approximate estimate of  $\Delta F^0 = 10$  to  $12$  Cal. made by Conant and Carlson (2) from the activation energies of enolization as measured by the temperature coefficient of the rate of racemization of certain ketones.

*For the keto form of phenol*



$\Delta F_{298}^0$  (enolization) =  $-18.6$  (wholly enolic)

For the hydroxy derivatives of furane (only known in the case of complex derivatives) one can estimate  $\Delta F^0$  (enolization of the keto form) of approximately  $-6.7 - (-2.5) = -4.2$  or  $K = 10^{-8}$ , essentially wholly enolic. If the combustion data for naphthalene and its hydrogenation products can be relied on, the unsaturation of the dicyclic system (in terms of  $\Delta F^0$  for one mole of hydrogen) is a few Calories less than that of furane; one would thus predict that the hydroxyl derivatives of naphthalene would be stable in the enolic form as, of course, they are. For a measurable equilibrium between the keto and enol forms,  $\Delta F^0$  (of enolization) should lie between about  $-3$  and  $+3$  and this in turn would mean a value of  $\Delta F^0$  of hydrogenation of the parent hydrocarbon of  $-9$  to  $-3$  (the corresponding  $\Delta H$  values being about  $-18$  and  $-12$ ). The phenylated ethylenes approach this range, and it is therefore not surprising that although modern work has shown that triphenylvinyl alcohol,  $(\text{C}_6\text{H}_5)_2\text{C}=\text{COHC}_6\text{H}_5$ , is in reality wholly the ketonic form,  $(\text{C}_6\text{H}_5)_2\text{CHCOC}_6\text{H}_5$ , nevertheless the compound so readily forms enolic derivatives that it was long regarded as enolic. The corresponding monophenyl and diphenyl derivatives do not show the same behavior.

The equilibrium between anthrone and anthranol in alcoholic solution is such that 80 per cent of the keto form is present (4). From this we may estimate that the value of  $\Delta H$  for hydrogenation of anthracene at the 9,10-position is approximately  $-15$  Cal., since the  $\Delta F^0$  of the tautomerization of the 9-hydroxyl derivative is about zero. This prediction we hope to test shortly by direct calorimetric measurements. If it is confirmed, it will place this addition reaction of anthracene between those of furane and cyclopentadiene, which is in accord with the fact that anthracene forms

a dibromide addition product when treated with bromine. Too few carbonyl compounds have been measured as yet to make it worth while to do more than draw attention to the rôle of the oxygen atom in influencing the affinity of the double bond. Judging from divinyl ether, methoxypropene, and crotonaldehyde, both the carbonyl and the *oxygen* of an ether linkage are capable of conjugation with neighboring double bonds; thus divinyl ether is approximately the equivalent of  $\text{CH}_2=\text{CH}-\text{CH}=\text{CH}-\text{CH}=\text{CH}_2$ . The quantitative measure of their action is about the same as for a carbon-carbon double bond, but an exception is found in vinyl acetate, for which a larger  $\Delta H$  value has been found than calculated even without conjugation. The decision as to whether this is generally connected with the second oxygen atom of the carboxyl group must await further work.

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# REACTIONS OF SOLUTIONS OF METALS IN LIQUID AMMONIA

W. CONARD FERNELIUS AND GEORGE W. WATT<sup>1</sup>

*Department of Chemistry, The Ohio State University, Columbus, Ohio*

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<sup>1</sup> Present address: The Goodyear Tire and Rubber Co., Akron, Ohio.



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## PART I. FOREWORD

### I. INTRODUCTION

The idea of a *solution* of a metal in a non-metallic solvent is one which the mind trained in chemistry and physics may ponder profitably. While these sister sciences have devoted much effort to the study of metals, have amassed a great fund of information concerning the characteristics and behavior of these interesting materials, and have developed elaborate theories to correlate the experimental data, the existence of simple solutions of metals in *non-metallic* solvents continues to impress many an otherwise well-informed person as a unique situation, the real importance of which only slowly dawns upon his consciousness. Yet systems of exactly this type with such solvents as liquid ammonia and the simple aliphatic amines are readily realized experimentally, have long been known, and have been the subject of numerous investigations. The study of the true nature of these solutions and of their chemical reactions has led

to important conclusions concerning the nature of the metallic state, intermetallic compounds, free radicals, organoalkali compounds, and certain reaction mechanisms, as well as the structural relationships of certain compounds. These solutions constitute one of the most effective reducing agents available and have become important synthetic reagents, especially for numerous organic compounds and for practically all substances in a highly reduced condition. The necessary techniques for handling such solutions have been developed and are comparatively easy to use. Surprisingly, only a beginning has been made in the study of metallic solutions, and the future holds much in store for those investigators who would proceed along paths already well marked and others only dimly suggested. One may state with certainty that these solutions will come to play an increasingly important rôle in organic syntheses and in the preparation of highly reduced inorganic compounds; and further, that they will prove useful in the study of intermediate stages of reduction.

The physical properties and nature of solutions of metals (84, 150, 160, 179, 188) have been discussed in detail in this journal and elsewhere, as well as some of the *general* aspects of the chemical reactions which these solutions exhibit (37, 151, 186). However, the many known reactions of these solutions have never been brought together in one place so that the wide usefulness and great possibilities of such systems may be clearly realized by one not thoroughly familiar with this field. The present writing is an attempt at a comprehensive review and somewhat critical discussion of the literature on reactions of metal solutions. This survey is prefaced by a short general review of the nature of solutions of metals to acquaint the reader with the character of the systems under discussion. Where references are given in this section they refer to recent work not covered in previous reviews. A few articles which have already appeared in this journal are closely related to certain portions of this review and may be consulted with profit in connection with it. The subjects of these articles are: (1) "The chemistry of the alkali amides" (18, 22); (2) "Metallic salts of alcohols and alcohol analogs" (73); and (3) "Organoalkali compounds" (388).

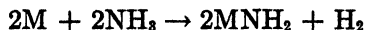
## II. SYSTEMS CONSISTING OF SOLUTIONS OF METALS IN NON-METALLIC SOLVENTS; STABILITY OF THESE SOLUTIONS

The alkali metals, lithium (165), sodium, potassium, rubidium, and cesium, are freely soluble in liquid ammonia without any considerable heat effect (231, 235) and without chemical reaction to form dark blue solutions which are much less dense than pure ammonia (161), conduct the electric current with great facility (80), and are strongly paramagnetic (104, 356). The early literature on these solutions is confusing and erroneous, in that

the solutions are taken to contain "metal ammoniums," definite combinations between metal and solvent, such as  $\text{NaNH}_2$ ,  $\text{Li} \cdot 4\text{NH}_3$ , and  $\text{Na}_2\text{N}_2\text{H}_6$ . Such combinations have been shown definitely not to exist but some workers, especially the French (117, 119, 257), have been loath to abandon the early view and references to "metal ammoniums" appear occasionally even in recent years.<sup>2</sup>

The alkaline-earth metals (calcium, strontium, and barium) are also markedly soluble in liquid ammonia to give the same blue solutions, but in these cases definite compounds,  $\text{M} \cdot 6\text{NH}_3$  (23, 24), analogous to salt ammonates rather than "metal ammoniums," are formed:  $\text{Ca}(\text{NH}_3)_6$  (174),  $\text{Sr}(\text{NH}_3)_6$  (328), and  $\text{Ba}(\text{NH}_3)_6$  (286). The physical properties of these solutions have not been extensively investigated. Magnesium likewise dissolves to a slight extent to give a pale blue solution.<sup>3</sup> While no other metals are definitely known to be soluble in liquid ammonia, it may be argued on the basis of certain chemical reactions that a few metals (beryllium (15), zinc (86), aluminum (6), gallium, lanthanum, cerium (10), and manganese (8)) also are soluble to a very slight extent. The tetra-substituted ammonium radicals, whose behavior closely resembles that of the alkali metals, impart a blue color to their liquid ammonia solutions (90, 173, 302, 332, 333).

Solutions of metals in liquid ammonia are remarkably stable, considering the extreme reactivity of the alkali and alkaline-earth metals with such solvents as water and the alcohols. Ammonia solutions of pure metals may be preserved for long periods (i.e., a couple of weeks in the case of sodium) even at room temperature. On long standing, especially at higher temperatures, amide formation becomes appreciable,



One may seek an explanation for this lack of reaction in the very small autoionization of liquid ammonia as compared to water, in the marked basicity (i.e., low proton availability) of liquid ammonia, and the relatively lower electrode potentials of these metals in liquid ammonia as compared to water (316). Such reaction, however, is markedly influenced by catalysts (5, 7, 14, 16, 17, 19, 38, 169, 360). Thus, an otherwise stable potassium solution is converted into the amide in from twenty minutes to an hour when a bit of iron oxide or finely divided platinum is present. Short ultra-violet light also catalyzes the reaction of the alkali metals with liquid ammonia (144, 300).

<sup>2</sup> All reactions in this paper are formulated in terms of the simple metals only, even when this involves rewriting the equations given in the original reference.

<sup>3</sup> Under special conditions  $\text{Mg}(\text{NH}_3)_6$  may be obtained (277a).

Metals are also soluble in some of the amines of low molecular weight: lithium (112, 292), sodium, potassium (111, 293), cesium (111, 319), and calcium (111, 293) are soluble in methylamine; lithium is less soluble in ethylamine than in methylamine (172); cesium (318) is soluble in ethylamine; sodium (172, 318), potassium (172), and calcium (318) are insoluble in ethylamine; lithium is insoluble in propylamine (172); cesium is soluble with reaction in isopropylamine (318); lithium, sodium, and potassium are insoluble in secondary and tertiary amines (172); lithium, sodium (81), potassium (172), and cesium (81) are soluble in ethylenediamine; in hydrazine lithium is slightly soluble, sodium is soluble but reactive, potassium is too reactive to note solubility, and calcium is insoluble (371, 372). These solutions of metals in amines have not been extensively studied. All are more or less unstable, owing to interaction between solvent and solute to produce hydrogen and substituted amides. Each of these solutions is blue in color, closely resembling ammonia solutions. In the case of methylamine, the light-absorption curves have been determined and are of somewhat different character than those of ammonia solutions (109). The molten alkali amides (82) and molten sodium hydroxide (83) also dissolve the alkali metals to give blue solutions. Calcium forms a similar blue solution in a molten mixture of sodium and potassium chlorides (108). Even water appears to form transitorily blue solutions of the alkali metals (383).

### III. THE NATURE OF SOLUTIONS OF METALS IN NON-METALLIC SOLVENTS

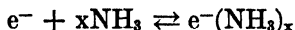
In many respects the properties of solutions of metals are intermediate in character between those of metals and those of electrolytic solutions, or perhaps one should say that these solutions constitute a connecting link between metallic and electrolytic conductors. Thus at high concentrations the atomic conductance of solutions of metals compares favorably with that of such metals as iron and strontium (220). In the more dilute region, on the other hand, solutions of metals exhibit the characteristics of electrolytes. The curve representing the variation of the temperature coefficient of conductance as a function of dilution also shows the same transition from that characteristic of a metal to that typical of electrolytes. Calculations (data from electromotive force of concentration cells) of the ratio of the transference numbers of negative to positive ions in liquid ammonia solutions of sodium show that, near saturation, the negative ion has a mean speed some two hundred eighty times that of the positive ion (178). This ratio diminishes with decreasing concentration until the relative carrying capacity becomes seven in the most dilute regions. Finally, the electrical conductance data show that the negative ion is the same for solutions of lithium, sodium, and potassium (the differ-

ence in the equivalent conductances of these solutions is due to the independently known different carrying capacities of the positive ions concerned) and that the conductances of dilute solutions of sodium and potassium and of sodium and lithium are practically additive (118). Also the light-absorption data show that, at equivalent concentrations, the absorption spectra of dilute solutions of lithium, sodium, potassium, cesium, magnesium, and possibly calcium are identical.

All of the facts known at present concerning solutions of metals in liquid ammonia may be harmonized by making two very simple assumptions: (1) In concentrated solution one may picture the metal atoms dissociating in accordance with the equation,



into the ordinary positive ions of salts of the metal and electrons. The electrons, however, have much the same mobility which they have in a solid, so that the solution possesses a very high conductance. (2) Upon dilution, the above dissociation is accompanied by a second reaction: i.e., the association of ammonia molecules with the electrons,



The mobility of the ammoniated electron is much less than that of the free electron. Thus, as the solution becomes progressively more and more dilute, more of the electrons are associated with ammonia until the conduction process becomes truly electrolytic in character. Further, it is readily seen that the negative ion of all metals in liquid ammonia is the same.

Although there are very few data on the subject, it is entirely reasonable to assume that solutions of metals in solvents other than ammonia have the same general character as those in ammonia.<sup>4</sup> It has been shown for methylamine that the metals are less ionized in this solvent than in ammonia and that the minimum in the molecular conductivity occurs at a somewhat higher concentration (113). Further, the solvation of electrons in methylamine is not as complete as in liquid ammonia, and diminishes as the temperature is increased.

With the above picture of the nature of metal solutions in mind, one may logically expect that the chemical reactions exhibited by these solutions will be of two types: (1) ionic double decomposition reactions and (2)

<sup>4</sup> There are some who regard these metal solutions as colloidal in character (301). Few, if any, of the properties of ammonia solutions of metals are in harmony with this point of view. More recently a modified form of the colloidal metal theory has been proposed (63), but neither the experimental work nor the theoretical interpretation is convincing.

reduction reactions. As will be seen in subsequent discussions, many examples of both types of reaction are known. In passing, mention should be made of the unusually favorable conditions presented by solutions of metals for carrying out reductions. It is universally recognized today that reduction consists in the addition of electrons to a given atomic system. Then a solution of electron-ions should be an extremely active reducing agent. Consider further that a *solution* of a metal eliminates one of the very serious limitations in the use of metals as reducing agents, i.e., surface area, by making it infinite. Add to this factor the marked solvent power of liquid ammonia for a great variety of substances (29, 41, 97, 103, 116, 156, 275) and the normally low reactivity of the solvent toward the dissolved metal, and it can easily be seen why so many reductions take place readily and rapidly in liquid ammonia. Indeed, the use of an excess of the reducing agent is the exception rather than the rule and, because of the high tinctorial power of dissolved metal, most reactions—even of a complicated character—can be *titrated* to a definite endpoint. Where the solvent power or reactivity of the ammonia (toward either the metal or the substance being reduced) are unsuited to a given reaction, then recourse to some of the simple amines may frequently be had.

#### IV. EXPERIMENTAL PROCEDURES INVOLVED IN THE STUDY OF REACTIONS OF SOLUTIONS OF METALS

No review of the reactions of metal solutions would be complete without some discussion of the techniques employed in handling these solutions. There are many reasons for making such a statement. It is certainly true that the development of methods for studying solutions in low-boiling solvents has been of extreme importance in leading to the present state of knowledge concerning reactions of metals. These techniques have become widely used and fairly well standardized. Despite the fact that on many occasions these techniques have been entirely inadequately described in the literature, there is really nothing about them which is so extremely difficult as to prevent the uninitiated from attempting to carry out reactions involving them. Further, these techniques are readily adaptable to a wide variety of differing experimental conditions and may be easy or more or less difficult depending upon the kind of results one desires. Finally some appreciation of the usefulness and limitations of the experimental methods is needed in order to evaluate properly the work of various investigators. In a careful reading of the literature on the reactions of metals in liquid ammonia, it is evident that much valuable information has been missed by the failure to realize the full possibilities of existing techniques.

Some of the considerations which govern the usage of the various tech-

niques so far developed are these. Ammonia is a low-boiling (normal boiling point,  $-33.35^{\circ}$ ), hygroscopic liquid. The metal solutions, some of the common reactants, and many of the products of reaction are sensitive to both air and water. Frequently gases (particularly hydrogen) are evolved during the reduction or subsequent reactions and arrangements should be made to collect these gases. On some occasions the reactants or reaction products, while much less volatile than ammonia, "steam-distill" with evaporating ammonia. The predominating practice has been to treat the final reaction products with ammonium salts, water, or alcohol. Such procedure frequently alters to a greater or lesser degree the primary products of the reaction, including by-products. In many cases, isolation, in relatively pure form, of one or more of the products of the reaction is desirable, since this may shed considerable light on the mechanism of the reaction, or show if simultaneous or consecutive side reactions are taking place.

The techniques for working with liquid ammonia solutions may be divided into two major groups: (1) reactions at low temperatures (atmospheric pressure or less) and (2) reactions under pressure (temperature from  $0^{\circ}\text{C.}$  to those in excess of  $100^{\circ}\text{C.}$ ). In either event it is necessary to decide first whether the commercial anhydrous ammonia is suitable or whether further purification is necessary. Most of the liquid on the market is a synthetic product made directly from its constituent elements. It is a remarkably pure material which is very nearly anhydrous, contains only slight amounts of non-condensable gas, and is free from any appreciable amount of volatile and condensible impurities as well as organic contamination (282). For many purposes, this product may be used directly. In most other cases, it is necessary only to store the liquid in the presence of sodium (sodium amide) to remove the last traces of water (153). The complete purification of ammonia has been studied by McKelvy and Taylor (282; cf. 4).

#### *A. Reactions at low temperatures*

The recommended apparatus for carrying out reactions at low temperatures (normal boiling point or below) in liquefied gases consists of numerous modifications of a single general type.<sup>5</sup> A system is constructed (preferably on a permanently mounted rack consisting of rigid horizontal and vertical iron rods) which consists of a reaction cell immersed in a cooling bath usually containing liquid ammonia or solid carbon dioxide and some organic liquid. The cell is so arranged that its contents may be observed visually and is equipped with certain fittings which permit of (1) condensa-

<sup>5</sup> For typical apparatus see references 115, 152, 195, 199, 202, 226, 228, 239, 375, and 394.

tion of purified ammonia, (2) stirring the reaction mixture, (3) stepwise or continuous addition of known or measurable amounts of reacting material (gaseous, liquid, or solid), and (4) collection of volatile products (normally accomplished by scrubbing out the ammonia with water, separating the condensible material, and, after suitable drying, etc., analyzing the insoluble gases). In many cases it is also advisable to arrange the system so that the cell may be evacuated and removed for weighing. Simple modifications may also be made to wash an insoluble material (35). The kinds of information which may thus be obtained from a simple study include reacting ratios, amount of excess reactant added, products formed including isolation of intermediates and purification, color changes, phases present and their appearance and disappearance, and by-products. More or less extensive modifications of the apparatus mentioned permit the determination of the conductance of solutions (209, 214) (including temperature coefficients) (221), transference numbers of ions (96), potentials of cells (177, 314, 415), electrode potentials (315), products of electrolysis (26, 91, 105, 176), absorption spectra of solutions (106, 110), solubility of compounds (103, 157, 167, 329), potentiometric changes during titration (407), density of solutions (158, 162, 200), molecular weights (76, 98, 335, 337), vapor pressure of solutions (159, 212), viscosity of solutions (87, 336), and heats of reaction and of solution (230, 231, 235, 338a).

There are many cases where the use of open Dewar vessels or even unjacketed flasks and beakers is not objectionable. In such cases, however, it is well to remember that, while the use of such procedures may save time and may make some manipulations a little easier, it also seriously limits the investigator in many operations, in that the reaction is not under as delicate control, the ingress of air and moisture may be definitely harmful, serious loss of volatile material may occur, and the study of intermediates and by-products is seriously hampered if not entirely prevented.

### *B. Reactions under pressure*

Under the leadership of Franklin, the use of sealed glass Faraday tubes for reactions at temperatures near that prevailing in the average laboratory has been perfected to a fine art (95, 154). This technique permits of a wide variety of operations such as visual observation, especially of intermediates, recrystallization and purification of moderately soluble products, purification of insoluble products by washing, freeing of soluble products from insoluble impurities, isolation of products for analysis or subsequent study *before* their destruction by water, etc., collection of gases evolved, freedom to alter the temperature at will over a wide range (slightly above room temperature to that of a mixture of carbon dioxide snow and ether), and ability to transfer the contents of one tube to another container.



Probably the greatest advantage of the Franklin technique is the marked solubility at room temperature of many substances which are only slightly soluble at the boiling point of ammonia.

While such a technique is ideally adapted for certain operations, it suffers a tremendous handicap in that the quantity of material which may be treated in this fashion is always rather small (not over a few grams) and also (assuming careful glass work and freedom from shock) in the constant danger of breakage of such tubes, especially if the internal pressure becomes much greater than that of liquid ammonia (viz., when a gas is liberated) or if the temperature rises. In many cases these limitations may be overcome by the use of autoclaves. Since liquid ammonia solutions of ammonium salts attack metals above hydrogen in the electrochemical series (11) and most metals act as catalysts for the conversion of the alkali metals to amides, autoclaves should be made of the less active metals (nickel, monel metal, etc.) or be glass-lined. They should also be equipped with a needle valve for filling with ammonia and for "blowing off" or collecting gases. By suitable modification, autoclaves may be fitted for conducting electrolyses, gradual addition of an ammonia solution of a reactant, extraction of a mixture of reaction products, etc.

Many investigators have been active in devising apparatus for carrying out the following operations with liquid ammonia solutions at or near room temperature: determination of potentials of cells (77), electroplating (26, 355), measurement of optical activity (340, 344), determination of the solubility of compounds (133, 275, 303, 341), molecular-weight determinations (342, 354), vapor-pressure measurements (134, 175, 255, 343), determination of viscosity (349), ultramicroscopic examination (410), and extraction of soluble products from solids (409).

For reactions above room temperature autoclaves may be used or a bomb which permits heating a sealed glass tube surrounded by liquid ammonia (25).

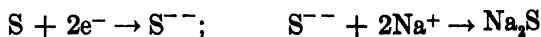
## PART II. INORGANIC REACTIONS

### I. INTRODUCTION

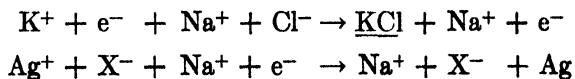
While water is well adapted as a medium in which to carry out reactions with strong oxidizing agents, it is not well adapted to carrying out reactions with strong reducing agents. The reducing power of reducing agents in water is limited by the fact that stronger reducing agents than hydrogen liberate hydrogen from water. Liquid ammonia suffers no such handicap, since the strongest reducing agents, the alkali metals, form stable solutions in this solvent. Thus, ammonia (and the simple amines) becomes the

ideal medium for the study of reduction reactions by means of strong reducing agents, a field which remains largely unexplored. Liquid ammonia is further of great usefulness because of its wide solvent power for electrolytes.

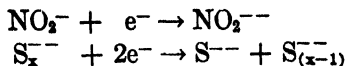
The process of reduction by means of metals in liquid ammonia consists essentially in the combination of an electron with an atom (or a group of atoms) or an ion. The positive ions of the metals are, of course, also present, but they take no part in the reduction process. The positive ions possess no metallic properties, and they are concerned in the process of reduction only to the extent of supplying the counterbalancing electrical charge for negative ions. When an atom undergoes reduction, a negative ion is formed,



When a positive ion is reduced a neutral atom or group is commonly formed,

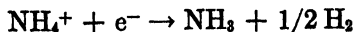


the course of the reaction being determined in most cases by the relative solubilities. A few cases are known where a negative ion undergoes reduction. In such cases an ion of higher charge or a number of ions are formed,

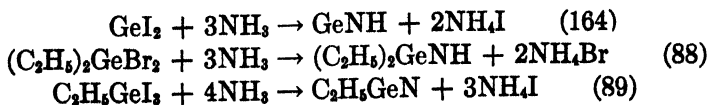


## II. AMMONIUM SALTS

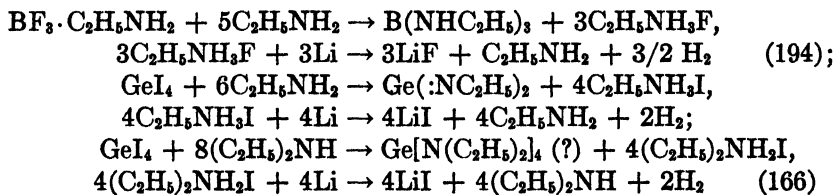
One of the simplest and most general reactions exhibited by solutions of metals is that with ammonium salts,



A summary of such reactions is given in table 1. The early observations on this reaction were prompted by a desire to isolate the ammonium radical (295, 296). Certain ammonolytic reactions have been brought to completion by neutralizing the ammonium salts with alkali metals. Among such reactions are:



The alkali metals have also been utilized in a similar capacity for certain reactions taking place in amines:



Sodium and potassium dissolve readily (room temperature) in an ammonia solution of ammonium nitrate (Divers' solution) without evolution of gas by reducing the nitrate to nitrite (75).

TABLE 1  
*Reactions of solutions of metals with ammonium salts*

AMMONIUM SALT	METAL	PRODUCT	REFERENCES
$\text{NH}_4\text{Cl}$ .....	Li	LiCl	295
	Ca	$\text{CaCl}_2$	295
$\text{NH}_4\text{Br}$ .....	Na	NaBr	88
$\text{NH}_4\text{I}$ .....	Na	NaI	89, 163
	Li	$\text{LiN}_3$	30
$\text{NH}_4\text{N}_3$ .....	Na	$\text{NaN}_3$	30
	K	$\text{KN}_3$	30
	Ca	$\text{Ca}(\text{N}_3)_2$	30
	Mg	$\text{Mg}(\text{N}_3)_2$	30
$\text{NH}_4\text{CN}$ .....	Ca	$\text{Ca}(\text{CN})_2 \cdot 2\text{NH}_3$	92
$(\text{NH}_4)_2\text{S}$ .....	Li	$\text{Li}_2\text{S}$	296
	Ca	CaS	296
$\text{NH}_4\text{C}_2\text{H}_3\text{O}_2$ .....	Na	$\text{NaC}_2\text{H}_3\text{O}_2$	243
$\text{NH}_4\text{SC}_4\text{H}_4$ .....	Na	$\text{NaSC}_4\text{H}_4$	243

### III. ELEMENTS

Solutions of metals in liquid ammonia react with a number of the elements. Reactions with those elements which are two to four places in front of a rare gas (in the long-period or Bohr-Thomsen arrangement of the elements) form a particularly interesting group. Each of these elements forms with the metals an ammonia-insoluble, white or slightly colored salt of a composition to be expected on the basis of the customary valence of the element ( $\text{Na}_2\text{S}$ ,  $\text{K}_3\text{Sb}$ ,  $\text{Na}_4\text{Sn}$ ) and one or more ammonia-soluble, strongly colored salts containing homoatomic anions (sometimes called polyanionic salts) ( $\text{Na}_2\text{S}_{2-5}$ ,  $\text{K}_3\text{Sb}_7$ ,  $\text{K}_4\text{Pb}_9$ ). The application to liquid ammonia solutions of potentiometric titration methods by Zintl and coworkers (406) has been very fruitful in determining the composition of

TABLE 2

*Reactions of solutions of metals in liquid ammonia with certain elements*

ELEMENT	METAL	COMPOUNDS FORMED	NOTES	REFERENCES
Oxygen.....	Na	NaOH, NaNH <sub>2</sub> , NaNO <sub>2</sub>	Slow reaction	140, 145, 252
		Na <sub>2</sub> O <sub>2</sub>	Rapid reaction	252
		Na <sub>2</sub> O <sub>3</sub>	Not confirmed	140*, 145*, 252
	K	KOH, KNH <sub>2</sub> , KNO <sub>2</sub>	Slow reaction	252
		K <sub>2</sub> O <sub>2</sub> , K <sub>2</sub> O <sub>4</sub>	Rapid reaction	140, 145, 229, 252
		K <sub>2</sub> O <sub>3</sub>	Not confirmed	140*, 145*, 252
	Rb	Rb <sub>2</sub> O <sub>2</sub> , Rb <sub>2</sub> O <sub>4</sub>	-60°C. (?)	322
	Cs	Cs <sub>2</sub> O <sub>2</sub> , CsNH <sub>2</sub> , CsOH, CsNO <sub>2</sub> , CsNO <sub>3</sub>	Slow reaction at -60°C.	320, 321
		Cs <sub>2</sub> O <sub>2</sub> , Cs <sub>2</sub> O <sub>3</sub> , Cs <sub>2</sub> O <sub>4</sub>	Rapid reaction at -60°C.	320, 321
	Ba	BaO, BaO <sub>2</sub>	Gelatinous pre- cipitate	120, 285
Sulfur . . .	Li	Li <sub>2</sub> S	White; very slight- ly soluble	13
		Li <sub>2</sub> S <sub>2</sub>	Yellow solution; slightly soluble	13
		Li <sub>2</sub> S <sub>4</sub>	Red solution	13
		Li <sub>2</sub> S <sub>x</sub>	Red solution	13
	Na	Na <sub>2</sub> S	White; very slight- ly soluble	13, 129, 131, 406
		Na <sub>2</sub> S <sub>2</sub>	Yellow solution; slightly soluble	13, 406
		Na <sub>2</sub> S <sub>3</sub>	Red solution	406
		Na <sub>2</sub> S <sub>4</sub>	Red solution	13, 406
		Na <sub>2</sub> S <sub>5</sub>	Red solution	129, 131, 406
		Na <sub>2</sub> S <sub>6</sub>	Red solution	406
		Na <sub>2</sub> S <sub>7</sub>	Red solution	406
		Na <sub>2</sub> S <sub>x</sub>	Red solution	13, 129
	K	K <sub>2</sub> S	White; very slight- ly soluble	13, 129, 131
		K <sub>2</sub> S <sub>2</sub>	Yellow solution; slightly soluble	13
		K <sub>2</sub> S <sub>4</sub>	Red solution	13
		K <sub>2</sub> S <sub>5</sub>	Red solution	129, 131
		K <sub>2</sub> S <sub>x</sub>	Red solution	13
	Ca	CaS (white, insoluble)	Ca in excess	294
		CaS <sub>x</sub> (red crystals)	S in excess	294

TABLE 2—Continued

ELEMENT	METAL	COMPOUNDS FORMED	NOTES	REFERENCES
Selenium . . .	Li	$\text{Li}_2\text{Se}$	White; very slightly soluble	13
		$\text{Li}_2\text{Se}_2$	Red solution	13
		$\text{Li}_2\text{Se}_3$	Green solution	13
		$\text{Li}_2\text{Se}_4$	Red solution	13
		$\text{Li}_2\text{Se}_5$	Red-green solution	13
	Na	$\text{Na}_2\text{Se}$	White; very slightly soluble	13, 128, 131, 406
		$\text{Na}_2\text{Se}_2$	Bright red solution	13, 406
		$\text{Na}_2\text{Se}_3$	Wine-red solution	13, 406
		$\text{Na}_2\text{Se}_4$	Green solution	13, 128, 129, 131, 406
		$\text{Na}_2\text{Se}_5$	Red-green solution	13, 406
	K	$\text{K}_2\text{Se}$	White; very slightly soluble	13, 128, 131
		$\text{K}_2\text{Se}_2$	Red solution	13
		$\text{K}_2\text{Se}_3$	Green solution	13
		$\text{K}_2\text{Se}_4$	Red solution	13, 128, 129, 131
		$\text{K}_2\text{Se}_x$	Red-green solution	13
Tellurium . . .	Na	$\text{Na}_2\text{Te}$	White precipitate; yellow solution	129, 131, 201, 208, 406, 6
		$\text{Na}_2\text{Te}_2$	Violet solution	201, 208, 40
		$\text{Na}_2\text{Te}_3$	Dark red solution	129, 131, 208, 406
		$\text{Na}_2\text{Te}_4(?)$		201, 208, 406
Nitrogen . . .	K	$\text{K}_2\text{Te}$	White; insoluble	129, 131
		$\text{K}_2\text{Te}_3$	Brown solution	129, 131
Phosphorus . .	Na, K		No reaction	142
		$\text{Na}_3\text{P}_2\text{H}_3 + 3\text{NaNH}_2$	Na in excess	126
	Na	$\text{NaP}_3 \cdot 3\text{NH}_3$	P in excess	125
Arsenic . . .	K	$\text{KP}_3 \cdot 3\text{NH}_3$	P in excess	125
	Na	$\text{Na}_3\text{As} \cdot \text{NH}_3$	With either Na or As in excess	127
	K	$\text{K}_3\text{As} \cdot \text{NH}_3$ $\text{K}_3\text{As}_4 \cdot \text{NH}_3$	K in excess As in excess	130 130
Antimony . . .	Li	$\text{Li}_3\text{Sb} \cdot \text{NH}_3$	With either Li or Sb in excess	259-61
	Na	$\text{Na}_3\text{Sb}$	Brown precipitate; yellow solution	139, 145
		$\text{Na}_3\text{Sb}_{1-7}$	Red-brown solution	306

TABLE 2—*Concluded*

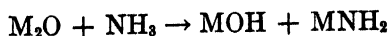
ELEMENT	METAL	COMPOUNDS FORMED	NOTES	REFERENCES
Bismuth. .	Na	Na <sub>3</sub> Bi	Black; insoluble	139, 145
Germanium .	See under GeS and GeS <sub>2</sub> , section VII			
Tin ..	Na		Soluble compound	306
	Li	Li <sub>4</sub> Pb <sub>x</sub>	Green solution	413
	Na	NaPb <sub>4</sub> ·2NH <sub>3</sub>	Green solution	138*
		NaPb	Solid, Na in excess	139
		NaPb <sub>2</sub>	Green solution	145, 171
		Na <sub>4</sub> Pb <sub>9</sub>		218, 347, 406
Lead	K	KPb <sub>2</sub>		139
		K <sub>4</sub> Pb <sub>9</sub> ·xNH <sub>3</sub>	Soluble compound	171
	Rb		Green solution	413
	Cs		Amethyst solution	413
	Sr		Brown-violet solution	413
			Insoluble	413
Mercury .	Na	NaHg <sub>8</sub>		138, 145
	K	KHg <sub>18</sub>		138, 145

\* The results or conclusions of this work have been modified by later investigation.

the various compounds which a given element may form. Bergstrom (9) has developed an electronegative replacement series based upon the ability of an element to displace another from liquid ammonia solutions containing the latter element in a homoatomic anion. The literature on these compounds is summarized in table 2. In many cases the earlier work has not been confirmed by subsequent study and such instances have been noted in the table.

Elements more than four places in front of a rare gas are not prone to react with solutions of metals when in compact form, but often do so when present in finely divided form, as when produced by reduction of solutions of their compounds (see below) (406).

*Oxygen.* In the case of oxygen the products are different depending upon whether the reaction is performed rapidly or slowly. When oxygen gas is conducted slowly through a solution of sodium or potassium (−33°C.), the monoxide first formed is ammonolyzed to an equimolecular mixture of the hydroxide and amide (253),

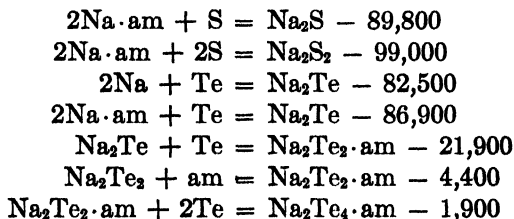


Subsequent oxidation converts the amide to nitrite,



The rapid oxidation of these metals produces the oxides  $\text{Na}_2\text{O}_2$ ,  $\text{K}_2\text{O}_2$ , and  $\text{K}_2\text{O}_4$  (no trioxides). Potassium tetroxide of 99 per cent purity may be formed at  $-50^\circ\text{C}$ .; at  $-33^\circ\text{C}$ . considerable amounts of potassium hydroxide and potassium nitrite are formed. Potassium dioxide, also of 99 per cent purity, may be formed at  $-50^\circ$  to  $-60^\circ\text{C}$ . by passing oxygen through the solution until the blue color disappears. At lower temperatures a colloidal sol and viscous solution are formed, while at higher temperatures there is reduction of the dioxide to the monoxide and consequent ammonolysis. The polyoxides are unique in that they are not soluble in liquid ammonia.

*Sulfur, selenium, and tellurium.* Vapor-pressure measurements of the sodium-tellurium complexes in liquid ammonia have shown that two sodium ions are associated with each complex tellurium ion,  $\text{Te}_x^{--}$  (256). The oxidation products in liquid ammonia ( $-33^\circ\text{C}$ .) of the sodium mono- and poly-sulfides, -selenides, and -tellurides have been determined (281). The heats of reaction ( $-33^\circ\text{C}$ .) of sodium solutions with sulfur and tellurium have recently been measured (231):



*Nitrogen, phosphorus, arsenic, antimony, and bismuth.* As might be expected, nitrogen is unreactive toward solutions of metals.<sup>6</sup> Advantage has been taken of the solubility of the alkali metals in extracting the excess sodium from such ammonia-insoluble compounds as  $\text{Na}_3\text{As}$ ,  $\text{Na}_3\text{Sb}$ , and  $\text{Na}_3\text{Bi}$  (258, 411a).

*Germanium, tin, and lead.* By electrolyzing solutions of sodium polyplumbide it has been shown that 2.26 gram-atoms of lead are deposited at the anode and dissolved at the cathode for each faraday of electricity passed (347). The energy of the reaction ( $-33^\circ\text{C}$ .),  $4\text{Na} + 9\text{Pb} \rightarrow \text{Na}_4\text{Pb}_9\cdot\text{am}$ , has been found to be  $-88,000$  cal. (231).

#### IV. HYDRIDES

Since the hydrides of the halogens and of sulfur combine with ammonia to form ammonium salts, these have already been discussed in section II, page 205. Even though the reaction of hydrides with metal solutions offers a fertile field of research, only a few of them have ever been studied.

<sup>6</sup> For reactions in liquid ammonia of a polyphosphide of the formula  $\text{Rb}_3\text{P}_n$ , see reference 27.

TABLE 3

*Reactions of halides of elements with solutions of metals in ammonia*

HALIDE USED	METAL	SUBSTANCE FORMED	NOTES	REFERENCES†
Group I				
CuI.....	Na	Cu		406
AgCl.....	Na	Ag		33a, 36, 37
AgI.....	Na	Ag		33a, 36, 37, 217, 406
AgI.....	Ca	Ag		33a
AgCN.....	Na	Ag		33a, 217
AgCN.....	Ca	CaAg		217
AgCN.....	Ca	Ag		33a
AuI.....	Na	NaAu		406
Group II				
ZnI <sub>2</sub> .....	Na	NaZn <sub>4</sub> NaZn <sub>12</sub> (?)		217 406
Zn(CN) <sub>2</sub> .....	Na	NaZn <sub>4</sub> Zn	If Zn(CN) <sub>2</sub> is in excess	34, 37, 217 34
Zn(CN) <sub>2</sub> .....	Ca	Ca <sub>7</sub> Zn		217
CdI <sub>2</sub> .....	Na	NaCd NaCd <sub>5-7</sub>		217 406
Cd(CN) <sub>2</sub> .....	Na	NaCd		217
HgI <sub>2</sub> .....	Ca	Ca <sub>3</sub> Hg <sub>2</sub>		217
Hg(CN) <sub>2</sub> .....	Na	NaHg	2NaHg → Na + NaHg <sub>2</sub>	217, 406
Hg(CN) <sub>2</sub> .....	Ca	Ca <sub>3</sub> Hg <sub>2</sub>		217
Group III				
BF <sub>3</sub> ·NH <sub>3</sub> .....	Na	H <sub>2</sub>	Reaction takes place in several steps	193
BF <sub>3</sub> ·N(C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> .....	Li	No action in (C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> N solution		193
	Na	No action in (C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> N solution		193
GaBr <sub>3</sub> ·6NH <sub>3</sub> .....	Na	Ga(?)		149
TlI.....	Na	Na <sub>3</sub> Tl <sub>2</sub> NaTl, NaTl <sub>2</sub>		217 406
Group IV				
SnI <sub>2</sub> .....	Na	Na <sub>4</sub> Sn Na <sub>4</sub> Sn <sub>x</sub>	Unstable	217, cf. 411a 217, cf. 406
	Ca	Ca <sub>3</sub> Sn		217



TABLE 3—*Concluded*

HALIDE USED	METAL	SUBSTANCE FORMED	NOTES	REFERENCES†
Group IV— <i>Concluded</i>				
PbBr <sub>2</sub> .....	Na		Heat of reaction*	231
PbI <sub>2</sub> .....	Na	Na <sub>4</sub> Pb	Unstable	217, cf. 411a
		Na <sub>4</sub> Pb <sub>7</sub>		406
		Na <sub>4</sub> Pb <sub>9</sub>	Dark green	406
	K	K <sub>4</sub> Pb <sub>9</sub>		406
	Ca	Ca <sub>2</sub> Pb <sub>3</sub>		217
ZrBr <sub>4</sub> .....	K	Black precipitate, red permanent	solution; neither	403
		Zr(NK) <sub>2</sub> ·NH <sub>3</sub> , H <sub>2</sub>	Secondary reactions	403
ThBr <sub>4</sub> .....	K	Th(NH)NK·NH <sub>3</sub> , H <sub>2</sub>	Slow reaction	403
		Th(NK) <sub>2</sub> ·KNH <sub>3</sub>	Continued action	403
Group V				
NI <sub>2</sub> ·3NH <sub>3</sub> .....	Na	NaI, N <sub>2</sub>		132
SbBr <sub>3</sub> .....	Na	NaSb <sub>4.3</sub>		217
BiCl <sub>3</sub> .....	Na	NaBi <sub>3.3</sub>		217
BiI <sub>3</sub> .....	Na	Na <sub>3</sub> Bi	Black precipitate	406
		Na <sub>3</sub> Bi <sub>3</sub>	Deep violet	406
		Na <sub>3</sub> Bi <sub>5</sub>	Brown	406
Group VII				
MnI <sub>2</sub> .....	Na	Mn	Probable initial reaction	37
		NaNH <sub>2</sub> , Mn(NH <sub>2</sub> ) <sub>2</sub>	Subsequent reactions	37
		Mn(NHNa) <sub>2</sub> ·2NH <sub>3</sub>		
		Mn	Highly reactive metal	276

\* PbBr<sub>2</sub>·am + 6Na = 2NaBr·am + Na<sub>4</sub>Pb - 104,400

PbBr<sub>2</sub>·am + 2Na = 2NaBr·am + Pb - 91,200

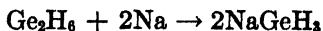
PbBr<sub>2</sub> + 2Na·am = 2NaBr·am + Pb - 123,700

† Important references, not otherwise mentioned, bearing upon the nature of salts of homoatomic anions (formed by elements two to four places in front of a rare gas) and of intermetallic compounds (or phases) (formed by elements more than four places in front of a rare gas) include the following: 12, 85, 155, 180, 182, 405, 408, 412.

Water reacts as it does with metals under other conditions. Phosphine reacts with both sodium and potassium in liquid ammonia to form substances of the formulas NaPH<sub>2</sub> and KPH<sub>2</sub>, respectively (143, 147). Germane reacts similarly with a solution of sodium (198),



Digermane also forms sodium trihydrogermanide (189),



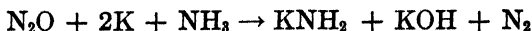
#### V. HALIDES (AND CYANIDES)

The products obtained by treating halides of elements with metal solutions (table 3) in most cases do not differ greatly from those obtained by direct reaction with the elements themselves, since the first step in the reduction of salts is undoubtedly the liberation of the free element. It appears, however, that the elements when so liberated are in a very reactive condition, since substances are produced under these circumstances which are not obtainable by direct reaction with the compact metal. The elements two to four places before a rare gas stand out in sharp contrast to the remainder of the elements. Among the former certain generalities have already been noted. For the latter group about all one can say is that when the element itself (silver, copper) is not precipitated, then some compound of an alkali or alkaline-earth metal with the element will be precipitated whose formula seemingly disobeys all valence rules and concerning which few generalities have as yet been discovered. This latter field is greatly in need of further investigation. Aside from the formation of the free element and of compounds of the element with the reducing metal, one other type of reaction is encountered. The element (metal) reduced may act as a catalyst for the conversion of the reducing metal to the amide which will react with the reduced element (manganese) or with the salt (zirconium, thorium).

#### VI. OXIDES

The compilation of data given in table 4 shows that investigations on the oxides of non-metals have not been extensive. Carbon monoxide forms carbonyls, which await further work to establish their structure definitely. Carbon dioxide seems to react with the ammonia to form carbamic acid (or ammonium carbamate), which then forms a sodium salt. The hydrogen thus liberated reduces a portion of the carbamate to formate.

The apparently complex mixture of products obtained by the action of nitrous oxide on metal solutions may be explained on the basis of two reactions. In the first, a molecule of the oxide is reduced to nitrogen gas:



the other products, alkali amide and hydroxide, are those which would be expected from ammonolysis of the alkali oxide (see page 209). The resulting amide then reacts with another molecule of the oxide in this fashion,



The latter reaction is known to take place under somewhat different conditions (72, 124, 382).

Nitric oxide reacts with solutions of metals to form precipitates having the composition  $\text{NaNO}$ ,  $\text{KNO}$ , and  $\text{BaN}_2\text{O}_2$  which, after dissolving in water, will give the characteristic silver salt of hyponitrous acid (142, 146, 284). Zintl and Harder (411), however, have shown, by means of Debye-Scherer photographs, that nitrosyl sodium,  $(\text{NaNO})_n$ , obtained from the interaction of nitric oxide and a solution of sodium, is not identical with sodium hyponitrite.

TABLE 4

*Reactions of non-metallic oxides with solutions of metals in ammonia*

OXIDE	METAL	PRODUCTS	NOTES	REFERENCES
CO.....	Li	$\text{LiCO}$	$-60^\circ\text{C.}$ , white precipitate	305
	Na	$\text{Na}(\text{CO})_2$	$-50^\circ\text{C.}$ , very explosive	141, 148
	K	$\text{K}(\text{CO})_2$	$-50^\circ\text{C.}$ , rose-white gelatinous precipitate	141, 148
	Rb	$\text{RbCO}$	$-60^\circ\text{C.}$ , white precipitate	305
	Ca	$\text{Ca}(\text{CO})_2$	$-60^\circ\text{C.}$ , white precipitate	305
	Ba	$\text{Ba}(\text{CO})_2$	$-50^\circ\text{C.}$ , gelatinous precipitate	120, 284
CO <sub>2</sub> .....	Na	$\text{H}_2\text{NCO}_2\text{Na}$	$-50^\circ$ to $-60^\circ\text{C.}$	317
		$\text{HCO}_2\text{Na}$ (due to H from above)	$-25^\circ$ to $-35^\circ\text{C.}$	317
N <sub>2</sub> O.....	Na	$\text{N}_2$ , $\text{NaOH}$ $\text{NaNH}_2$	Primary reaction	142, 146
	K	$\text{NaN}_3$ , $\text{NaOH}$	Reaction of $\text{N}_2\text{O}$ with amide	142, 146
		see Na		142, 146
NO.....	Na	$\text{NaNO}$ $(\text{NaNO})_n$	Gelatinous precipitate	142, 146 411
	K	$\text{KNO}$	Gelatinous precipitate	142, 146
	Ba	$\text{BaN}_2\text{O}_2$	Gelatinous precipitate	284
NO <sub>2</sub> .....	Ba	$\text{BaN}_2\text{O}_2$	Gelatinous precipitate	120

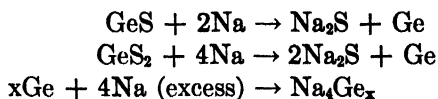
Nitrogen dioxide, while not fully investigated, is seemingly reduced by a solution of barium and forms the same material as nitric oxide (120).

The reduction of only a few oxides of the metals has been studied. Bergstrom (17) apparently observed no reduction of ferric and cobaltous-cobaltic oxides ( $\text{Fe}_2\text{O}_3$  and  $\text{Co}_3\text{O}_4$ ) by a liquid ammonia solution of potassium. A general study of the behavior of oxides of metals toward a solution of potassium (370) at room temperature has shown that the oxides of

bismuth ( $\text{Bi}_2\text{O}_3$ ), tin ( $\text{SnO}$  and  $\text{SnO}_2$ ), lead ( $\text{PbO}$  and  $\text{PbO}_2$ ), zinc ( $\text{ZnO}$ ), and cadmium ( $\text{CdO}$ ) give intermetallic compounds, while silver oxide ( $\text{Ag}_2\text{O}$ ) furnishes the free metal. Cupric oxide is quantitatively reduced to cuprous oxide which, because of its marked catalytic effect upon the conversion of metal to amide, undergoes only slight reduction to metallic copper. Germanic oxide ( $\text{GeO}_2$ ) remains unchanged after long contact with a solution of potassium.

#### VII. SULFIDES

The sulfides of germanium are reduced by a solution of sodium in liquid ammonia ( $-33^\circ\text{C}.$ ) to sodium sulfide and sodium polygermanide (166a),



The potentiometric titration of arsenious sulfide ( $\text{As}_2\text{S}_3$ ) and antimonous sulfide ( $\text{Sb}_2\text{S}_3$ ) by sodium in liquid ammonia shows the following compounds:  $\text{Na}_3\text{As}$  (brown precipitate),  $\text{Na}_3\text{As}_2$  (yellow),  $\text{Na}_3\text{As}_3$  (dark red-brown), and  $\text{Na}_3\text{As}_7$ ;  $\text{Na}_3\text{Sb}$  (gray-brown precipitate),  $\text{Na}_3\text{Sb}_3$  (deep red), and  $\text{Na}_3\text{Sb}_7$  (406).

#### VIII. NITRIDES AND IMIDES

Germanous imide,  $\text{GeNH}$ , does not react with an ammonia solution of sodium at  $-33^\circ\text{C}.$  (164).

The reaction of nitrogen iodide has already been discussed under the heading of halides (page 213).

#### IX. TERNARY COMPOUNDS

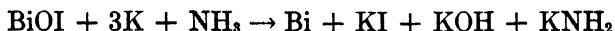
Despite the manifest opportunities for investigation presented by the field of ternary compounds, few such substances have been investigated. The outstanding case is that of sodium nitrite which forms a substance of the formula  $\text{Na}_2\text{NO}_2$ , variously known as disodium nitrite (279) and sodium hydronitrite (414). Similar reduction of sodium nitrite occurs using lithium and potassium and also of potassium nitrite using sodium.

Cobalt, nickel, cupric, and ferric nitrates are reduced by sodium in liquid ammonia ( $-33^\circ\text{C}.$ ) to the very finely divided and highly reactive metals (277). The particular technique used in these cases did not permit the isolation of any other products of these reactions.

No reduction of the cyanate ion takes place even in the presence of excess sodium and potassium, but appreciable reduction results when an excess of calcium is used. The thiocyanate ion, however, is partially re-

duced to sulfide and cyanide by sodium and potassium and completely reduced by calcium (33a).

Bismuth oxyiodide, BiOI, is reduced by solutions of sodium and potassium at room temperature according to the equation (370):



If excess alkali metal is present insoluble ( $\text{K}_3\text{Bi}$ ) and soluble ( $\text{K}_3\text{Bi}_2$ ) bismuthides are formed.

### PART III. ORGANIC REACTIONS

#### I. INTRODUCTION

While it is certainly true that the reactions of metal solutions with organic substances have been more extensively studied than those with inorganic substances, it is also true that in many cases less is known concerning the mechanism of the organic reactions, by-product formation, etc. This situation is in large measure due to the greater complexity of the organic reactions, but in part is due also to failure of the synthetic chemist, in his desire to obtain a final product, to concern himself greatly either with the steps involved in the synthesis or with the influence of experimental conditions upon the yield or stability of the various intermediates. What has already been said about the failure of many investigators to take full advantage of existing techniques applies with particular force to those who have studied reactions of metals with organic substances. One may point to several cases where, with only slight modification of the apparatus or even with more complete use of the apparatus at hand, much additional valuable information might readily have been obtained.

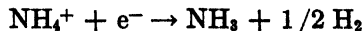
Liquid ammonia is an ideal medium for carrying out reduction reactions, not alone because certain metals dissolve to form stable solutions but likewise because of the wide solubility of organic compounds in this solvent. In this latter respect liquid ammonia resembles most closely the lower alcohols (41, 97). The use of diluents, such as petroleum ether, benzene, ether, and amines, in reductions has been suggested on several occasions (70, 359, 376, 400). Not only are such diluents of value in altering solubility relationships and rates of reaction, but in some cases they seem to have a directive influence upon the course of the reaction. The behavior of such mixed solvents has not been fully investigated nor are the factors involved definitely understood.

It is well to recall that the active principle of a metal solution is the free electron, and that the reactions exhibited by these solutions are essentially those of the electron. In the case of organic compounds, the reactions of metals may, for convenience, be classified roughly into a number of types.

1. *Displacement of an equilibrium involving an organic compound, the solvent, and an ammonium salt.* Such reactions have already been discussed in section II of part II. Whenever a substance is ammonolyzed to form even a small amount of an ammonium salt,

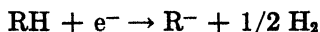


the resulting equilibrium may be displaced completely to the right by removing the ammonium ion through reaction with a metal solution,

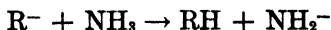


What has been said here concerning liquid ammonia applies equally well to the amines when used as solvents.

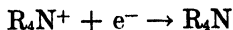
2. *Displacement of hydrogen.* Many of the reactions of organic compounds with solutions of metals are simply those of the displacement by a metal of active hydrogen from such compounds as  $HC\equiv CH$ ,  $(C_6H_5)_3CH$ ,  $ROH$ ,  $RNH_2$ , acids and their derivatives, with the resulting formation of salts,



The hydrogen is not always liberated in the molecular form, however, and may serve to reduce a portion of the original compound. When this occurs there are then two competing reducing tendencies, i.e., (1) that of the electron and (2) that of the hydrogen. Careful study of a few such cases should serve to distinguish between the two reductants and to determine if and when hydrogen may be expected to reduce a compound that is not reduced by the metal. Salts formed by metals under one set of conditions may not be stable under another set, such as an increase in temperature. Under such circumstances ammonolysis may result,



3. *Metal addition.* There are a number of occasions where the electron apparently adds directly to a molecule or ion. Such a reaction is encountered in the electrolysis of tetrasubstituted ammonium salts,



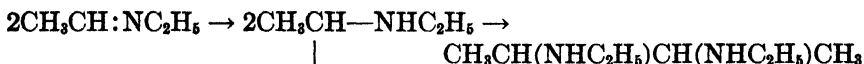
For solutions of metals, such reactions are usually of two types.

(a) *Addition to double bonds.* Addition of electrons to a double bond would be expected to result in the formation of a doubly charged ion,

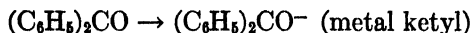


which may be stable under the experimental conditions or may be partially or completely ammonolyzed. Such reactions are known for C:C (phenyl-

substituted ethylenes, higher benzenoid hydrocarbons, etc.), C:O, C:N, C≡N, N:O, and N:N. Here again the information available is meager, since all possibilities have not been fully studied. In a few cases only one electron adds at a double bond. In such cases either one of two things may result: (1) a dimerization of the reduction product,

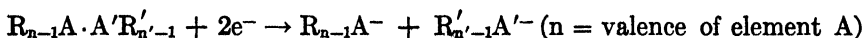


or (2) formation of a compound containing an element in an unusual state of valence,

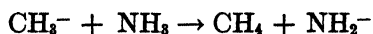


(b) *Addition to free groups.* Most of the free radicals so far studied react with electrons to form ions. Thus,  $\text{R}_3\text{C}$ ,  $\text{R}_3\text{Si}$ ,  $\text{R}_3\text{Ge}$ , and  $\text{R}_3\text{Sn}$  form singly charged anions and  $\text{R}_2\text{Ge}$  and  $\text{R}_2\text{Sn}$  form doubly charged anions. In the latter cases, a single equivalent of an alkali metal produces anions of the types  $\text{R}_2\text{Ge} \cdot \text{GeR}_2^-$  and  $\text{R}_2\text{Sn} \cdot \text{SnR}_2^-$ .

4. *Bond rupture.* In many instances the reducing action of a metal solution is of such a nature as actually to rupture a linkage between two atoms and for the electron to combine with each of the resulting fragments (cf. 74):

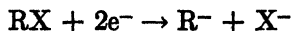


Some ions, such as methide and ethide, formed in this manner are not stable under the experimental conditions and are ammonolyzed,

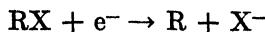


Instances of such bond rupture are known for the following cases: carbon-carbon, germanium-germanium, tin-tin, carbon-germanium, carbon-tin, silicon-germanium, silicon-tin, carbon-oxygen, germanium-oxygen, tin-oxygen, carbon-nitrogen, tin-nitrogen, sulfur-sulfur, carbon-sulfur, mercury-carbon, and carbon-halogen (see following paragraph). Undoubtedly a thorough investigation would disclose more types. (Some of these have been mentioned previously under the topic "addition to free groups.")

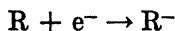
5. *Removal of halogen.* The reactions of solutions of metals with halogen compounds are essentially bond ruptures, but for convenience may better be considered separately. According to the general equation given above one would expect the following reaction to take place with organic halides,



In cases where the organic radical R is capable of existence as a free group, the following reaction takes place,



Further action may convert the free group into an ion,



Probably it is well to look upon all reactions of halogens as proceeding in accordance with the two steps given. Thus there are likely to be present during the reduction of a halogen compound, in addition to the reactants and halide ions, both negative organic ions and free groups. In many cases the ions are unstable and ammonolyze, thus introducing amide ion,  $NH_2^-$ , into the system. Organic halogen compounds are reactive toward the amide ion to form either unsaturated hydrocarbons or amines. The latter and certain of the former form salts with metals, and these salts react with the halogen compound. The more reactive of the free groups may react either with the solvent or with themselves (Wurtz-Fittig synthesis). Thus it is easy to see that reductions of this type may become exceedingly complex (fortunately this does not happen often), and that it is very essential to examine all possibilities in order to learn just what is taking place in the reaction. Two cases are known of a hydrocarbon radical isomerizing in the formation of an ion.

6. *Removal of other elements.* In a few cases so far investigated, metals in solution are able to remove an oxygen atom from organic combination ( $C_6H_5NO_2$  and  $C_6H_5N(:O):NC_6H_5$ ). When this occurs the sodium oxide resulting is ammonolyzed to an equimolecular mixture of sodium hydroxide and sodium amide,



7. *Catalysis by solutions of metals.* Occasionally solutions of metals exert a catalytic effect upon a reaction (polymerization of styrene and interaction between triethylsilane and ethylamine).

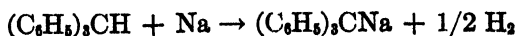
## II. HYDROCARBONS

### A. Saturated hydrocarbons

There is no recorded instance of any reaction between a saturated hydrocarbon and a solution of a metal, nor is there any reason on the basis of known reactions in liquid ammonia to expect any such reaction.

### B. Phenyl-substituted saturated hydrocarbons

Metallic sodium and potassium dissolved in liquid ammonia ( $-33^\circ C.$ ) directly displace hydrogen from triphenylmethane (184, 216, 232, 241),





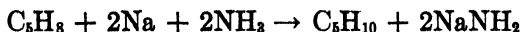
although the reactions take place slowly and the pure alkali salts may be more readily obtained by using the alkali amides (20, 390).

Diphenylmethane reacts slowly and incompletely with a liquid ammonia solution of sodium (room temperature) to give some of the sodium salt (271).

Wooster and Mitchell (393) have studied the action of potassium in liquid ammonia ( $-33^{\circ}\text{C}.$ ) upon phenyl-substituted methanes and ethanes. They observed no reaction with  $\text{C}_6\text{H}_5\text{CH}_3$ ,  $(\text{C}_6\text{H}_5)_4\text{C}$ ,  $\text{C}_6\text{H}_5\text{CH}_2\text{CH}_3$ , and  $\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{C}_6\text{H}_5$ ; slight reaction with  $(\text{C}_6\text{H}_5)_3\text{CCH}_3$  and  $(\text{C}_6\text{H}_5)_3\text{CCH}_2\text{C}_6\text{H}_5$ ; and formation of intense red or orange-yellow alkali salts with  $(\text{C}_6\text{H}_5)_2\text{CH}_2$ ,  $(\text{C}_6\text{H}_5)_3\text{CH}$ ,  $(\text{C}_6\text{H}_5)_2\text{CHCH}_2\text{C}_6\text{H}_5$ , and  $(\text{C}_6\text{H}_5)_2\text{CHCH}(\text{C}_6\text{H}_5)_2$ . Under similar conditions potassium ruptures a carbon-carbon bond in  $(\text{C}_6\text{H}_5)_3\text{CC}(\text{C}_6\text{H}_5)_3$  (see section D below). The alkali metal salts of hydrocarbons readily react with alkyl and aryl halides, and are thus useful synthetic reagents.

### *C. Ethylenic hydrocarbons*

The simple ethylenic hydrocarbons are not reactive toward solutions of metals in liquid ammonia: e.g., amylene (269) and cyclohexene (404). When isoprene reacts with a solution of sodium in ammonia ( $-33^{\circ}\text{C}.$ ) there is formed 2-methyl-2-butene in 60 per cent yield,



as well as hydrocarbons of high molecular weight. The 2-methyl-2-butene is not further reduced by an excess of sodium-ammonia reagent (287) (see section D, following).

### *D. Phenyl-substituted ethylenic hydrocarbons*

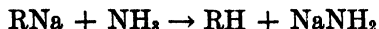
The reduction of a number of phenyl-substituted olefins with alkali metals in liquid ammonia solution has been studied. The results are summarized in table 5 (reactions at  $-33^{\circ}\text{C}.$  unless otherwise noted).

These data, together with those given in sections B and C above, have been carefully examined by Wooster and Ryan (399), who have pointed out the various types of reactions involved: (1) displacement of hydrogen; (2) addition to a double bond; (3) polymerization; (4) dimerization; (5) cleavage of carbon-carbon bonds; and (6) addition to but one of two double bonds in a molecule. In the case of derivatives of saturated hydrocarbons, reaction takes place to any considerable extent when, and only when, the compound contains the benzohydril group,  $(\text{C}_6\text{H}_5)_2\text{CH}-$ . Many of the organoalkali compounds which might logically be considered as inter-

TABLE 5  
Reduction of phenyl-substituted olefins with alkali metals in liquid ammonia

OLEFIN	METAL	PRODUCTS REPORTED	NOTES	REFERENCES
$C_6H_5CH=CH_2$ . . . . .	Na	$C_6H_5C_2H_5$ (50 per cent) + styrene polymers, $NaNH_2$	1.34, 1.38 equivalents of sodium react, slow reaction	266, 273, 398
$C_6H_5CH=CHC_6H_5$ . . . . .	Na, K	$C_6H_5CH_2CH_2C_6H_5$ , $MNH_2$ (M = Na or K)	Intermediate red color; persists for a long time	398, 404
	Na (-78°C.)			331
	Na (room temperature)		Ammonolysis immediate	270
	Na	$(C_6H_5)_2CNACH_3$ , $NaNH_2$ , $(C_6H_5)_2CNACH_2CH_2CNa$ ( $C_6H_5$ ) <sub>2</sub> (10 to 30 per cent)		398
$(C_6H_5)_2C=CH_2$ . . . . .	Na (low temperature)	$(C_6H_5)_2CNACH_3$ , + small amount 1,1,4,4-tetraphenylbutane	Toluene diluent	404
$(C_6H_5)_2C=CHCH_3$ . . . . .	Na, K	$(C_6H_5)_2CMCH_2C_6H_5$ , $MNH_2$		393, 397, 398
$(C_6H_5)_2C=C(C_6H_5)_2$ . . . . .	Na	$(C_6H_5)_2CNACH_2C_6H_5$ , and $(C_6H_5)_2CHNa$ or $(C_6H_5)_2CNCH_2(?)$	When in excess, 3.65 equivalents of sodium react	393, 398
$(C_6H_5)_2C=CHCH_3$ . . . . .	Na, K	$(C_6H_5)_2CMCH_2CH_3$ , $MNH_2$	Reacts readily	397, 398
$(C_6H_5)_2C=CH-CH_2C_6H_5$ . . . . .	Na (low temperature)	$(C_6H_5)_2CNACH_2CH_2C_6H_5$		404
$(C_6H_5)_2C=CHCH(C_6H_5)_2$ . . . . .	Na	$(C_6H_5)_2CNACH_2CH(C_6H_5)_2$ , $NaNH_2$		398
$(C_6H_5)_2C=C=C(C_6H_5)_2$ . . . . .	Na, K	$(C_6H_5)_2CMCH_2CM(C_6H_5)_2$ , $MNH_2$	Reacts readily; 3.76, 4.3 equivalents of sodium react	398

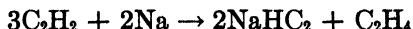
mediates in the reactions given in table 5 are not found because such substances are ammonolyzed,



In general, the alkali metal atoms are replaced by hydrogen except when they are present in the grouping  $(\text{C}_6\text{H}_5)_2\text{CM}-$  ( $\text{M} = \text{alkali metal}$ ). When the organoalkali compounds are stable in liquid ammonia they are useful synthetic reagents.

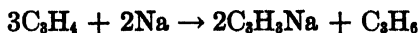
### *E. Acetylenic hydrocarbons*

When acetylene is passed into liquid ammonia solutions ( $-40^\circ$  to  $-60^\circ\text{C}.$ ) of lithium, sodium, potassium, calcium (291), rubidium, and cesium (297), the corresponding monoalkali acetylides,  $\text{MHC}_2$ , are formed. At the same time a limited amount of the acetylene is reduced to ethylene,



Magnesium is attacked by an ammonia solution of acetylene to form magnesium acetylide,  $\text{Mg}(\text{HC}_2)_2 \cdot 7\text{NH}_3$  (from  $2^\circ$  to  $-60^\circ\text{C}.$ ) and  $\text{Mg}(\text{HC}_2)_2 \cdot 5\text{NH}_3$  (above  $2^\circ\text{C}.$ ) (66). Monosodium acetylide and calcium acetylide have been used by a number of investigators for the preparation of substituted acetylenes (28, 123, 135, 170, 257, 264, 265, 280a, 283, 307-9, 358, 389). Because of the reduction of acetylene accompanying its reaction with sodium, Picon (310) prefers to use sodium amide to generate sodium acetylide.

The monosubstituted acetylenes also react with ammonia solutions of metals to form the corresponding salts and ethylenic hydrocarbons in the ratio 2:1,



Such reactions are reported for allylene, *n*-hexyne, heptyne, and octyne (265). Phenylacetylene gives the salt and ethylbenzene with sodium in ammonia (266, 273),



### *F. Aromatic hydrocarbons*

The benzene nucleus is not attacked by ammonia solutions of metals (269, 331, 393). Benzene, toluene<sup>7</sup>, xylene, etc., may be used advantageously as diluents for the reactions between metal solutions and many organic compounds (404) or for introducing a solution of a solid into

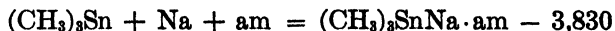
<sup>7</sup> For precautions see reference 391a.

ammonia (402). Naphthalene, however, is reduced by sodium and potassium solutions to tetrahydronaphthalene, with the concomitant formation of sodium amide (267, 331, 401). When this reaction is carried out at low temperatures ( $-33^{\circ}\text{C}$ . or lower) a bright red solution results. This color may be regarded as due to a relatively unstable intermediate organoalkali compound. Wooster and Smith (401) have examined the reaction in detail and have shown that the intermediate is the 1,2,3,4-tetrasodium addition product, but that even at  $-33^{\circ}\text{C}$ . this compound is three-fourths ammonolyzed. Other hydrocarbons similarly reduced are the following: anthracene (9,10-dihydroanthracene) (269, 290), phenanthrene (tetrahydrophenanthrene), acenaphthene (tetrahydroacenaphthene), biphenyl (tetrahydrobiphenyl) (269), and dimethylfluorene (tetrahydrodimethylfluorene) (271). When sodium or potassium is added to a liquid ammonia solution of 9,10-diphenylanthracene the 9,10-dialkali salts are formed (bright cherry-red solution, brick-red amorphous precipitate) (135a). Both fluorene and indene react with ammonia solutions of sodium to form sodium salts by substitution accompanied by some hydrogenation (268). An ammonia solution of fluorene reacts with magnesium (66).

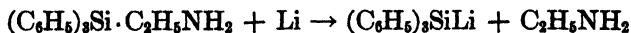
The following compounds do not react with metal solutions: terpinene, terpinolene, carvene,  $\alpha$ -pinene, and menthene (269).

*G. Free radicals. Substituted stanno- and germano-methanes and -ethanes*

*1. Free radicals.* Sodium solutions react with the free radical triphenylmethyl (hexaphenylethane) to produce sodium triphenylmethide (215). Similar reactions take place with other free groups: triphenylgermanyl (hexaphenylgermanoethane) (192, 205, 213, 227, 237), triphenylstannyl (hexaphenylstannoethane) (213), and trimethylstannyl (hexamethylstannoethane) (181, 183, 210, 236). That the electron in the trimethylstannomethide ion is not firmly held is shown by the following energy equation (235),

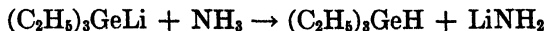


Triphenylsilyl forms an addition compound with ethylamine,  $(\text{C}_6\text{H}_5)_3\text{Si} \cdot \text{C}_2\text{H}_5\text{NH}_2$ , which does not react with sodium in liquid ammonia to an appreciable extent. In liquid ethylamine the following reaction occurs (203):



Triethylsilyl shows no reaction with sodium in liquid ammonia or with lithium in ethylamine (225). Triethylgermanyl (hexaethylgermanoethane) reacts with lithium in ethylamine to form lithium triethylger-

manide. The latter compound is partially aminolyzed in ethylamine and completely ammonolyzed in liquid ammonia,

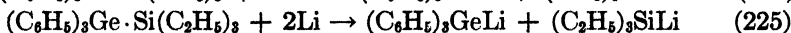


Potassium triethylgermanide prepared similarly in ethylamine is stable in liquid ammonia (204).

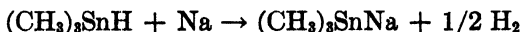
Tin and germanium form a type of free group which carbon does not form, i.e., dimethylstannyl,  $[(\text{CH}_3)_2\text{Sn}]_x$  (207), diphenylstannyl,  $[(\text{C}_6\text{H}_5)_2\text{Sn}]_x$  (62), and diphenylgermanyl,  $[(\text{C}_6\text{H}_5)_2\text{Ge}]_4$  (192). Each of these substances reacts with a solution of sodium to form the corresponding disodium salt:  $(\text{CH}_3)_2\text{SnNa}_2$ ,  $(\text{C}_6\text{H}_5)_2\text{SnNa}_2$ , and  $(\text{C}_6\text{H}_5)_2\text{GeNa}_2$ . In two of these cases intermediate substances,  $\text{NaSn}(\text{CH}_3)_2 \cdot \text{Sn}(\text{CH}_3)_2\text{Na}$  and  $\text{NaGe}(\text{C}_6\text{H}_5)_2 \cdot \text{Ge}(\text{C}_6\text{H}_5)_2\text{Na}$ , respectively, are known to form first. All of the salts mentioned above may be employed for synthetic purposes. By using them it has been found possible to prepare hydrides, alkyl and aryl derivatives, and chains of tin and germanium atoms: e.g., octaphenylgermanopropene,  $(\text{C}_6\text{H}_5)_3\text{Ge} \cdot \text{Ge}(\text{C}_6\text{H}_5)_2 \cdot \text{Ge}(\text{C}_6\text{H}_5)_3$ , and dodecamethylstannopentane,  $(\text{CH}_3)_3\text{Sn}[\text{Sn}(\text{CH}_3)_2]_3\text{Sn}(\text{CH}_3)_3$ .

For reactions of the dimethylgallium group see section H.

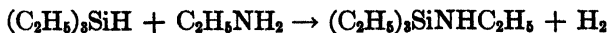
2. *Substituted ethanes.* Closely allied to the reactions given above are those between sodium and trimethylstannyltriphenylsilane in liquid ammonia and that between triphenylgermanyltriethylsilane and lithium in ethylamine (greater solubility of the silane):



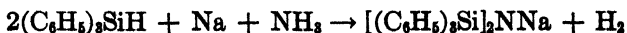
3. *Trisubstituted methanes.* Sodium in liquid ammonia reacts with trimethylstannane (183, 206) and triphenylstannane (61) to produce the sodium salt and hydrogen,



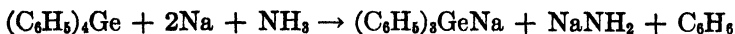
The sodium salt of triphenylstannane is in small part converted to the disodium salt,  $(\text{C}_6\text{H}_5)_3\text{SnNa}_2$ . Triethylgermane appears not to react with sodium in liquid ammonia (204). Triphenylgermane on the other hand gives the sodium salt and hydrogen but not quantitatively, since some of the disodium salt is formed (205). While lithium in ethylamine solution has no direct action on triethylsilane, the metal does serve as a catalyst for the homogeneous reaction (225),



The chief products of the reaction between triphenylsilane and sodium in liquid ammonia are sodium bis(triphenylsilyl)imide,  $[(\text{C}_6\text{H}_5)_3\text{Si}]_2\text{NNa}$ , and hydrogen (323),

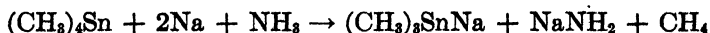


4. *Tetrasubstituted methanes.* Methyl- and *n*-propyl-triphenylgermane are not attacked by sodium in liquid ammonia (237). Tetraethylgermane, which is practically insoluble in liquid ammonia, shows no appreciable reaction with sodium in that solvent (204). Tetraphenylgermane, on the other hand, slowly reacts as follows:



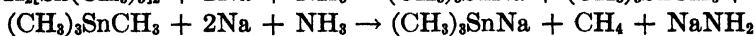
With a concentrated sodium solution, a second phenyl group is substituted by sodium to form  $(\text{C}_6\text{H}_5)_2\text{GeNa}_2$  (205).

Tetramethylstannane undergoes the following reaction with an ammonia solution of sodium (223, 236),

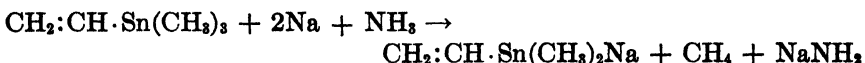
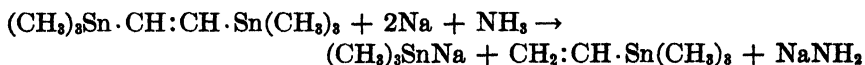


Tetraphenylstannane reacts similarly, with the exception that some of the sodium triphenylstannide is further substituted, forming the disodium compound (61).

Reactions with somewhat different types of compounds are those with bis(trimethylstannyl)methane and bis(trimethylstannyl)ethylene. The former reacts according to the equations (223):

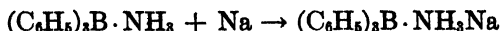


and the latter according to the following equations (224):

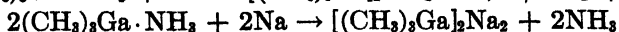
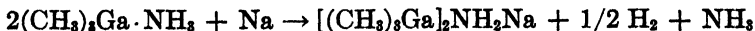


#### H. Trisubstituted derivatives of boron and gallium

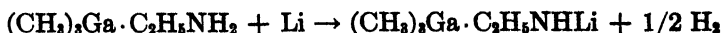
Triphenylboron ammine reacts with sodium in liquid ammonia thus (185):



The reaction of trimethylgallium ammine with sodium in liquid ammonia is in accord with the equations:



Depending on conditions, reaction takes place according to the first equation to the extent of from 60 to 100 per cent of the total gallium and according to the second from 30 to 0 per cent. A similar reaction takes place when trimethylgallium is treated with lithium in ethylamine, except that the first reaction is replaced by the following (238):



## III. HALOGEN COMPOUNDS

## A. The liquid ammonia-sodium method for determining halogens in organic compounds

Elements of the halogen family are removed quantitatively from all types of organic combination by solutions of metals in liquid ammonia. This fact constitutes the basis for one of the most convenient and rapid methods for determining organic halogen (including fluorine) (57, 65, 67, 68, 359). Those interested in the analytical determination of halogen have

TABLE 6  
*Reactions of alkyl halides with sodium in liquid ammonia*

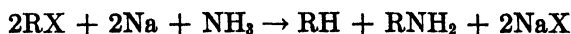
ALKYL HALIDE	PRODUCTS	REFERENCES
CH <sub>3</sub> Cl.....	CH <sub>4</sub>	256
CH <sub>3</sub> I.....	CH <sub>4</sub> , CH <sub>3</sub> NH <sub>2</sub> , NaCl (1)	42, 54, 263
C <sub>2</sub> H <sub>5</sub> Br.....	CH <sub>4</sub> , CH <sub>3</sub> NH <sub>2</sub> , NaI	54
	C <sub>2</sub> H <sub>6</sub> , NaBr, NaNH <sub>2</sub> (2)	387
	C <sub>2</sub> H <sub>6</sub>	262
C <sub>2</sub> H <sub>5</sub> I.....	C <sub>2</sub> H <sub>6</sub> , C <sub>2</sub> H <sub>5</sub> NH <sub>2</sub> , NaI (1)	263
	C <sub>2</sub> H <sub>6</sub> (75 per cent), C <sub>2</sub> H <sub>4</sub> (4 per cent), C <sub>2</sub> H <sub>5</sub> NH <sub>2</sub> (21 per cent), NaNH <sub>2</sub>	54
n-C <sub>4</sub> H <sub>9</sub> Cl.....	C <sub>4</sub> H <sub>10</sub> , C <sub>4</sub> H <sub>8</sub> (trace), NaNH <sub>2</sub>	54
	C <sub>4</sub> H <sub>10</sub> , C <sub>4</sub> H <sub>9</sub> NH <sub>2</sub> , NaI (1)	246, 263
n-C <sub>4</sub> H <sub>9</sub> I.....	C <sub>4</sub> H <sub>10</sub>	262
	C <sub>4</sub> H <sub>10</sub> (71 per cent), C <sub>4</sub> H <sub>8</sub> (7 per cent), C <sub>4</sub> H <sub>9</sub> NH <sub>2</sub> (21 per cent), NaNH <sub>2</sub>	54
n-C <sub>6</sub> H <sub>13</sub> Cl.....	C <sub>6</sub> H <sub>14</sub> , NaNH <sub>2</sub> , NaCl	40
iso-C <sub>6</sub> H <sub>13</sub> Cl.....	C <sub>6</sub> H <sub>14</sub> , C <sub>6</sub> H <sub>12</sub> (trace), NaNH <sub>2</sub>	54
iso-C <sub>6</sub> H <sub>13</sub> I.....	C <sub>6</sub> H <sub>14</sub> (70 per cent), C <sub>6</sub> H <sub>12</sub> (15 per cent), C <sub>6</sub> H <sub>13</sub> NH <sub>2</sub> (15 per cent), NaNH <sub>2</sub>	54
iso-C <sub>8</sub> H <sub>17</sub> Cl.....	C <sub>8</sub> H <sub>18</sub> , C <sub>8</sub> H <sub>16</sub> (trace), NaNH <sub>2</sub>	54
iso-C <sub>8</sub> H <sub>17</sub> I.....	C <sub>8</sub> H <sub>18</sub> , C <sub>8</sub> H <sub>16</sub> (trace), NaNH <sub>2</sub>	54
tert-C <sub>4</sub> H <sub>9</sub> I.....	sec-pentane (and explosion)	246
C <sub>2</sub> H <sub>5</sub> CHI(CH <sub>2</sub> ) <sub>2</sub> CH <sub>3</sub> .....	C <sub>6</sub> H <sub>14</sub> , C <sub>6</sub> H <sub>12</sub> (trace), NaNH <sub>2</sub>	54
CH <sub>3</sub> (CH <sub>2</sub> ) <sub>2</sub> CHICH <sub>2</sub> .....	C <sub>6</sub> H <sub>14</sub> , NaNH <sub>2</sub>	54

not concerned themselves with the fate of the hydrocarbon part of the molecule. It is sufficient to say that tars are sometimes encountered, and that polyhalogen compounds are very likely to form some cyanide. Compounds forming cyanide are the following: chloroform, bromoform (not iodoform), carbon tetrachloride, chloral and bromal hydrates, ethylidene chloride, tetrachloroethylene, and acetylene tetrachloride. Although the amount of cyanide thus formed is variable, it can be removed readily prior to determining the halogen. The liquid ammonia-sodium method is not quantitative for cyanide in nitriles.

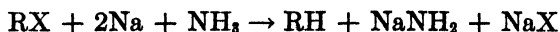
*B. Alkyl halides*

The monohalogen substitution products of the paraffin hydrocarbons react with a solution of sodium in liquid ammonia to form hydrocarbons, both saturated and unsaturated, sodium halides, and sodium amide, as table 6 shows.

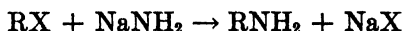
The reactions marked (1) in table 6 proceed in the following manner,



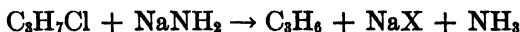
and those marked (2) proceed thus,



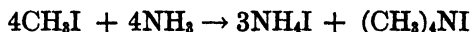
It seems that sodium amide is a constant product of most of these reactions, perhaps after the fashion of (2) above and that it reacts either to ammonolyze the alkyl halide,



or to remove hydrogen halide,



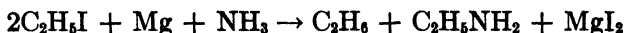
Sodium amide has been shown to enter into both types of reaction (21). The reaction of methyl iodide is complicated by the fact that this substance reacts readily with liquid ammonia to form tetramethylammonium iodide,



Sodium reacts readily with the ammonium iodide so formed (55),



Magnesium reacts with ethyl iodide in the following manner (251):



For reactions of halogen-substituted ketones see section VIII.

*C. Phenyl-substituted alkyl halides*

The data relative to the reactions of phenyl-substituted paraffin halides are assembled in table 7. The reaction of  $\beta, \beta, \beta$ -triphenylethyl chloride (marked \*) is interesting in that it involves a rearrangement of the hydrocarbon nucleus. The similar rearrangement of  $\gamma, \gamma, \gamma$ -triphenylpropyl iodide (marked \*\*) is accompanied by a spontaneous cleavage of a carbon-carbon bond.



*D. Unsaturated halides*

On reaction with a solution of sodium in liquid ammonia acetylene dibromide yields a variable amount of acetylene gas and sodium acetylide.

TABLE 7

*Reactions of phenyl-substituted alkyl halides with metals in liquid ammonia*

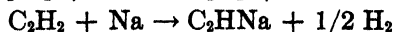
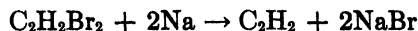
HALIDE	METAL	PRODUCTS	REFERENCES
$C_6H_5CH_2Cl$ .....	Na	$C_6H_5CH_3$ , $C_6H_5CH_2CH_2C_6H_5$ , and a solid hydrocarbon	69, cf. 247
$C_6H_5CH_2Br$ .....	Na	Bibenzyl	393
	K	Bibenzyl	393
$(C_6H_5)_2CHCl$ .....	Na	$(C_6H_5)_2CHCH(C_6H_5)_2$ (65.6 per cent), $(C_6H_5)_2CH_2$ (27.6 per cent)	69, 71
	Na	$(C_6H_5)_3CNa$	215
$(C_6H_5)_3CCl$ .....	K	$(C_6H_5)_3CK$	215
	Ca	Unstable reddish-brown com- pound	215
$C_6H_5CHCl_2$ .....	Na	Bibenzyl (7.3 per cent), benzyl- amine (37.6 per cent)	69
$(C_6H_5)_2CCl_2$ .....	Na	Tetraphenylethylene (90 per cent)	69, 71
$C_6H_5CCl_3$ .....	Na	Bibenzyl (5 per cent), nitrog- enous substance	69
$C_6H_5CH_2CH_2Br$ .....	Na	$C_6H_5C_2H_5$ (38.3 per cent), sty- rene (1.3 per cent)	69
$(C_6H_5)_3CCH_2Cl$ .....	Na	$(C_6H_5)_3CNaCH_2C_6H_5^*$	395, 397
$(C_6H_5)_3CCH_2CH_2I$ .....	Na	$(C_6H_5)_3CNa$ , $C_6H_5^{**}$	396
$C_6H_5(CH_2)_3Br$ .....	Na	$C_6H_5C_6H_7$ (28.2 per cent), $C_6H_5(CH_2)_3NH_2$ (17.9 per cent)	69
$C_6H_5(CH_2)_4Br$ .....	Na	$C_6H_5C_6H_9$ (43.1 per cent), $C_6H_5(CH_2)_4NH_2$ (16.5 per cent), unsaturated and other saturated hydrocarbons, other amines	69

TABLE 8

*Reactions of bromoolefins with sodium in liquid ammonia*

SUBSTANCE	MOLES USED		MOLES OBTAINED		ACETYLENE OLEFIN
	Olefin	Sodium	Acetylene	Olefin	
1-Bromo-1-propene.....	0.167	0.202	0.006	0.818	0.012
1-Bromo-1-octene.....	0.167	0.221	0.034	0.075	0.45
1,1-Dibromo-1-propene.....	0.167	0.389	0.050	0.070	0.71
1,1-Dibromo-1-octene.....	0.167	0.374	0.052	0.029	1.80

The products may be accounted for qualitatively if the following reactions are thought of as taking place in varying proportions (247):



Bachman (2) gives a table (table 8) summarizing his findings on the reactions of bromoolefins with sodium in liquid ammonia.

TABLE 9

*Reactions of halogenated olefins with sodium in liquid ammonia*

ORGANIC HALIDE	MOLES OF SODIUM USED	PRINCIPAL PRODUCT IDENTIFIED	YIELD IN PER CENT
$\beta$ -Bromostyrene. ....	2	Phenylacetylene	96
$\alpha$ -Chlorostyrene. ....	2	Phenylethane	15
<i>p</i> -Methyl- $\alpha$ -chlorostyrene. ....	2	Tolylacetylene	63
Stilbene dibromide. ....	15	Bibenzyl	73
Styrene dibromide ..	3	Phenylacetylene	66
2-Bromo-1-decene. ....	2	1-Decene	56

TABLE 10

*Reactions of paraffin polyhalides with solutions of sodium in liquid ammonia*

HALIDE	PRODUCTS	REFERENCES
$\text{CH}_2\text{Cl}_2$ .. ....	$\text{CH}_4$ (55 per cent), $\text{NaNH}_2$ , $\text{NaCl}$	46, 56
$\text{CHCl}_3$ .. . . .	$\text{CH}_4$ , $\text{NaNH}_2$ , $\text{NaCl}$ , small amounts of $\text{C}_2\text{H}_4$ , $\text{C}_2\text{H}_2$ , and $\text{NaCN}$	43
$\text{CHI}_3$ .. . . .	$\text{CH}_4$ , $\text{NaI}$ , some $\text{C}_2\text{H}_4$ , $\text{C}_2\text{H}_2$ , $\text{NaCN}$ , $\text{H}_2$ , and $\text{N}_2$	43
$\text{CCl}_4$ ... . . . .	$\text{CH}_4$ , $\text{NaCl}$ , $\text{NaCN}$ , small amount of $\text{N}_2$	43, 65
$\text{CH}_2\text{ClCH}_2\text{Cl}$ .....	$\text{C}_2\text{H}_4$ , $\text{NaCl}$ (*)	46, 56, 247
$\text{CH}_3\text{CHCl}_2$ .....	$\text{C}_2\text{H}_6$ (51 per cent), $\text{C}_2\text{H}_4$ (5 per cent), $\text{NaNH}_2$	46, 56
$\text{C}_2\text{Cl}_4$ ... . . . .	$\text{NaCN}$ (not confirmed)	65, cf. 67
$\text{CH}_3\text{CH}_2\text{CHCl}_2$ .. . . .	$\text{C}_2\text{H}_6$ , some $\text{C}_2\text{H}_4$	46
$\text{CH}_3\text{CCl}_2\text{CH}_3$ .....	$\text{C}_2\text{H}_6$ (64 per cent), $\text{C}_2\text{H}_4$ (14 per cent), $\text{NaNH}_2$ , $\text{NaCl}$	46, 56
Propylene dibromide.....	$\text{C}_2\text{H}_6$ , $\text{NaBr}$ (*)	46, 56
Isobutylene dibromide. ....	$\text{C}_4\text{H}_{10}$ , $\text{NaBr}$ (*)	56, 65
$\text{C}(\text{CH}_2\text{Br})_4$ .....	$\text{C}(\text{CH}_2\text{NH}_2)_4$ (small amounts)	117

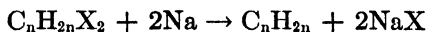
The monobromoolefins give principally the corresponding acetylenes and olefins, in a ratio, A/O, which increases with increasing length of the hydrocarbon chain. Under similar conditions the dibromoolefins also yield acetylenes and olefins, but high molecular weight polymers are formed at the same time and make up a considerable portion of the products. The ratio A/O is larger for the dibromoolefins than for the corresponding monobromoolefins, and also increases with increasing length

of the hydrocarbon chain. Small amounts of saturated hydrocarbons arise in all cases, owing to reduction of the olefins and acetylenes by the hydrogen formed in the reaction.

Vaughn (357) has examined the reaction of a number of halogenated olefins with sodium in liquid ammonia. His results are given in table 9. The acetylenes formed in no case were entirely free from hydrogenation products. Hence these reactions are not suitable for the preparation of pure acetylenes.

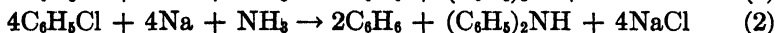
#### *E. Paraffin polyhalides*

The products of the reactions of various paraffin polyhalides with liquid ammonia solutions of sodium are given in table 10. It is to be noted that some of the reactions are somewhat complex. Those marked (\*) follow essentially the course,



#### *F. Aryl halides*

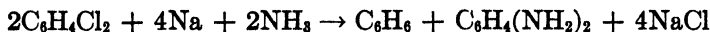
The action of aromatic halides with solutions of metals has been studied but very little. The principal products of the reaction between sodium and chlorobenzene or iodobenzene in liquid ammonia are benzene, diphenylamine, triphenylamine, and sodium halide (374). The following equations suggest the course of the principal reactions:



A small quantity of aniline is formed in accordance with the equation:

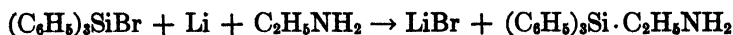


Using petroleum ether as a diluent, the predominating tendency becomes the formation of tertiary amine. Ortho- and para-chlorotoluene seem to react according to equation 3 above and the action of magnesium on iodobenzene follows the same course (248). *o*-Bromoxylene reacts slowly with sodium solution to form *o*-xylene and a nitrogen-containing residue (69). *o*-Dichlorobenzene and sodium react thus (249):

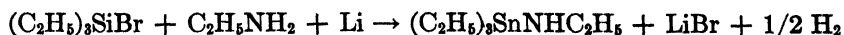


#### *G. Organohalides of silicon, germanium, tin, gallium, and mercury*

As much as from five to six atomic equivalents of sodium are consumed when triphenylsiliclyl chloride is treated with an excess of sodium in liquid ammonia. It is evident that the phenyl-silicon linkage is broken in this treatment (234). Triphenylsiliclyl bromide and metallic lithium react in ethylamine solution according to the equation (203),

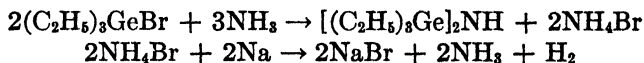


While lithium does not act upon triethylsilicyl bromide in ethylamine solution, it does serve to neutralize the products of the aminolysis of the bromide and thus to bring the following reaction to completion (225):

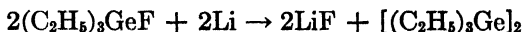


Triethyl-, tripropyl-, tributyl-, and triamyl-silicyl fluorides do not react with sodium in liquid ammonia at its boiling point (114).

Sodium triphenylgermanide has not been prepared by the action of the metal upon a triphenylgermanium halide, but only by the action of the metal upon hexaphenylgermanoethane. The reaction of sodium with diphenylgermanium dichloride must be carried on in an inactive solvent, since the chloride is ammonolyzed in liquid ammonia. Lithium in ethylamine solution acts upon diphenylgermanium dichloride to give a substance which retains ethylamine and which cannot be purified (192). Sodium does not act upon triethylgermanyl bromide in liquid ammonia, but instead reacts with the products of ammonolysis of the bromide:



Similar reactions take place between lithium and triethylgermanyl chloride and bromide in ethylamine. Under the same conditions the fluoride has less tendency to ammonolyze and hence may be reduced,

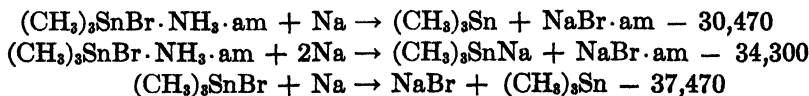


The reaction is unsatisfactory for the preparation of the digermane, however, since it seems to be complicated by the formation of lithium triethylgermanide (204).

Sodium in liquid ammonia reacts with triphenylstannyl bromide (61) and iodide (31, 32) to form sodium triphenylstannide. The trimethylstannide may be similarly prepared by the action of sodium on the corresponding bromide (32, 196, 223, 236) or chloride (206). If only one equivalent of sodium is used, this same reaction may be utilized to obtain a nearly quantitative yield of hexamethylstannoethane,



Sodium also converts dimethylethylstannyl bromide into the corresponding stannide (33). From measurements of the heats of reaction in liquid ammonia solution the following energy equations may be written (235):



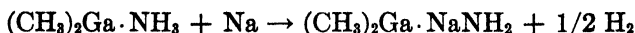
Diphenyltin dibromide (61) and diiodide (32) on treatment with sodium solution are converted into the free group diphenyltin,  $(C_6H_5)_2Sn$ , or the

salt, disodium diphenylstannide,  $\text{Na}_2\text{Sn}(\text{C}_6\text{H}_5)_2$ , depending upon the amount of sodium used. Similarly, dimethyltin dibromide is converted into the dimethyltin group,  $(\text{CH}_3)_2\text{Sn}$ , disodium dimethylstannide,  $(\text{CH}_3)_2\text{SnNa}_2$  (32, 207), or disodium tetramethylstannoethane,  $\text{NaSn}(\text{CH}_3)_2 \cdot \text{Sn}(\text{CH}_3)_2\text{Na}$  (222), depending upon the reacting ratios.

Dimethylgallium chloride,  $(\text{CH}_3)_2\text{GaCl}$ , is reduced to dimethylgallium when treated with one atomic equivalent of sodium in liquid ammonia. The free dimethylgallium combines with ammonia and may be obtained as a solid at  $-33^\circ\text{C}$ ., where an internal oxidation-reduction takes place slowly (rapidly at room temperature) according to the equation,



When dimethylgallium chloride is treated with two atomic equivalents of sodium, dimethylgallium is first formed, which reacts slowly with sodium, presumably according to the equation,



In this compound the amide ion is linked to gallium by a coördinate linkage (238).

Ethylmercuric chloride reacts slowly with sodium in liquid ammonia according to the following equation (219),



#### IV. ALCOHOLS AND PHENOLS

The alcohols react readily with the alkali metals in liquid ammonia with the evolution of hydrogen and the formation of alkoxides (44, 240). Secondary and tertiary alcohols react more slowly than primary alcohols. The resulting alkoxides are more soluble in the former cases (44). In many cases it seems that the alcohols do not react completely with sodium or potassium, but instead form compounds of the type  $\text{C}_2\text{H}_5\text{ONa} \cdot \text{C}_2\text{H}_5\text{OH}$  (44, 379). The alkoxides of the alkaline-earth metals may also be prepared by reaction between solutions of these metals and alcohols (49). Salts of the polyhydric alcohols are formed in the same manner as salts of the monohydric alcohols. With but few exceptions only one of the hydrogen atoms is displaced by the metal (45, 52, 58). The preparation of salts of unsaturated alcohols is accompanied by reduction on the primary alcohol grouping (or the double bond) (47, 48, 58),



Phenols react with solutions of the alkali metals in the same manner as the aliphatic alcohols. The naphthols, on the other hand, are in part reduced

TABLE 11

*Salts of alcohols, phenols, and naphthols prepared by reactions with solutions of metals in liquid ammonia*

ALCOHOL	SALT FORMED	REFERENCES	NOTES
Monohydric saturated alcohols			
CH <sub>3</sub> OH . . . . .	CH <sub>3</sub> OLi	58	
	CH <sub>3</sub> ONa	58	
	CH <sub>3</sub> OK	58	
	(CH <sub>3</sub> O) <sub>2</sub> Ca	50, 58	
	(CH <sub>3</sub> O) <sub>2</sub> Sr	58	
	(CH <sub>3</sub> O) <sub>2</sub> Ba	50, 58	
C <sub>2</sub> H <sub>5</sub> OH . . . . .	C <sub>2</sub> H <sub>5</sub> OLi	58	White precipitate More soluble than C <sub>2</sub> H <sub>5</sub> ONa
	C <sub>2</sub> H <sub>5</sub> ONa	58, 240, 379	
	C <sub>2</sub> H <sub>5</sub> OK	58, 379	
	(C <sub>2</sub> H <sub>5</sub> O) <sub>2</sub> Ca	50, 58	
	(C <sub>2</sub> H <sub>5</sub> O) <sub>2</sub> Sr	50, 58	
	(C <sub>2</sub> H <sub>5</sub> O) <sub>2</sub> Ba	50, 58	
n-C <sub>3</sub> H <sub>7</sub> OH . . . . .	C <sub>3</sub> H <sub>7</sub> ONa	361	Appreciably sol- uble Insoluble
n-C <sub>4</sub> H <sub>9</sub> OH . . . . .	C <sub>4</sub> H <sub>9</sub> ONa	240, 361	
	C <sub>4</sub> H <sub>9</sub> OK	379	
iso-C <sub>4</sub> H <sub>9</sub> OH . . . . .	C <sub>4</sub> H <sub>9</sub> OLi	58	
	C <sub>4</sub> H <sub>9</sub> ONa	58	
	C <sub>4</sub> H <sub>9</sub> OK	58	
	(C <sub>4</sub> H <sub>9</sub> O) <sub>2</sub> Ca	50	
n-C <sub>5</sub> H <sub>11</sub> OH . . . . .	C <sub>5</sub> H <sub>11</sub> ONa	361	
	(C <sub>5</sub> H <sub>11</sub> O) <sub>2</sub> Ca	50	
iso-C <sub>5</sub> H <sub>11</sub> OH . . . . .	C <sub>5</sub> H <sub>11</sub> OLi	58	
	C <sub>5</sub> H <sub>11</sub> ONa	58	
	C <sub>5</sub> H <sub>11</sub> OK	58	
	(C <sub>5</sub> H <sub>11</sub> O) <sub>2</sub> Ca	58	
Menthol:			
C <sub>10</sub> H <sub>19</sub> OH . . . . .	C <sub>10</sub> H <sub>19</sub> ONa	45	
Borneol:			
C <sub>10</sub> H <sub>17</sub> OH . . . . .	C <sub>10</sub> H <sub>17</sub> ONa	45	
Monohydric substituted alcohols			
Benzyl alcohol:			
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> OH . . . . .	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> OK	379	
Phenylpropyl alcohol:			
C <sub>6</sub> H <sub>5</sub> (CH <sub>2</sub> ) <sub>2</sub> CH <sub>2</sub> OH . . . . .	C <sub>6</sub> H <sub>5</sub> (CH <sub>2</sub> ) <sub>2</sub> CH <sub>2</sub> ONa	47	
Polyhydric saturated alcohols			
Glycol: (CH <sub>2</sub> OH) <sub>2</sub> . . . . .	CH <sub>2</sub> OH · CH <sub>2</sub> OLi	45, 52, 58	Stable in excess Na; insoluble (CH <sub>2</sub> OK) <sub>2</sub> etc. by heating the solid
	CH <sub>2</sub> OH · CH <sub>2</sub> ONa	45, 52, 58, 338, 379	
	CH <sub>2</sub> OH · CH <sub>2</sub> OK	45, 52, 58	
Glycol . . . . .	(CH <sub>2</sub> O) <sub>2</sub> Ca	52, 58	

TABLE 11—Continued

ALCOHOL	SALT FORMED	REFERENCES	NOTES
Polyhydric saturated alcohols—Concluded			
Glycerol: $\text{CH}_2\text{OH} \cdot \text{CHOH} \cdot \text{CH}_2\text{OH} \dots\dots\dots$	$\text{CH}_2\text{OH} \cdot \text{CHOH} \cdot \text{CH}_2\text{ONa}$	45, 334, 338	
Erythritol: $\text{CH}_2\text{OH} \cdot (\text{CHOH})_2 \cdot \text{CH}_2\text{OH} \dots\dots\dots$	Di-Li salt Mono-Na salt Ca salt 1:1	58 45, 58 58	
Mannitol: $\text{CH}_2\text{OH} \cdot (\text{CHOH})_4 \cdot \text{CH}_2\text{OH} \dots\dots\dots$	Di-Li salt Mono-Na salt Mono-K salt	58 45, 58, 334 45, 58, 334	
Unsaturated primary alcohols			
Allyl alcohol: $\text{CH}_2\text{:CHCH}_2\text{OH} \dots\dots\dots$	$\text{CH}_2\text{:CHCH}_2\text{ONa}$	47, 58	$\text{C}_3\text{H}_6$ (50 mole per cent of $\text{C}_3\text{H}_7\text{OH}$ ), no $\text{H}_2$ , no reduction of $\text{C:C}$ , $\text{NaOH}$
Citronellol: $(\text{CH}_3)_2\text{C:CH}(\text{CH}_2)_2\text{-CH}(\text{CH}_3)\text{CH}_2\text{-CH}_2\text{OH} \dots\dots\dots$	Mono-Na salt	47	
Geranioöl: $(\text{CH}_3)_2\text{C:CH}(\text{CH}_2)_2\text{-C}(\text{CH}_3)\text{:CHCH}_2\text{OH} \dots\dots\dots$	Mono-Na salt	58	$\text{C}_{10}\text{H}_{18}$ , $\text{NaOH}$
Linaloöl: $(\text{CH}_3)_2\text{C:CH}(\text{CH}_2)_2\text{-C}(\text{CH}_3)\text{OHCH:CH}_2 \dots\dots\dots$	Na salt	58	$\text{C}_{10}\text{H}_{18}$ , $\text{NaOH}$
Cinnamic alcohol: $\text{C}_6\text{H}_5\text{CH:CHCH}_2\text{OH} \dots\dots\dots$	$\text{C}_6\text{H}_5\text{CH:CHCH}_2\text{ONa}$ Some $\text{C}_6\text{H}_5(\text{CH}_2)_2\text{-CH}_2\text{ONa}$	48, 58	Some $\text{C}_6\text{H}_5\text{CH:-CHOH}$ , and $\text{C}_6\text{H}_5(\text{CH}_2)_2\text{CH}_2$
Phenols			
Phenol: $\text{C}_6\text{H}_5\text{OH} \dots\dots\dots$	$\text{C}_6\text{H}_5\text{ONa}$	210, 240, 379	Stable in excess Na
	$\text{C}_6\text{H}_5(\text{OH})\text{ONa}$	379	Very soluble
	$\text{C}_6\text{H}_4(\text{ONa})_2$	379	Rather insoluble
Resorcinol: $m\text{-C}_6\text{H}_4(\text{OH})_2 \dots\dots\dots$			(none of the disodium salts of dihydroxybenzenes is appreciably soluble (191))

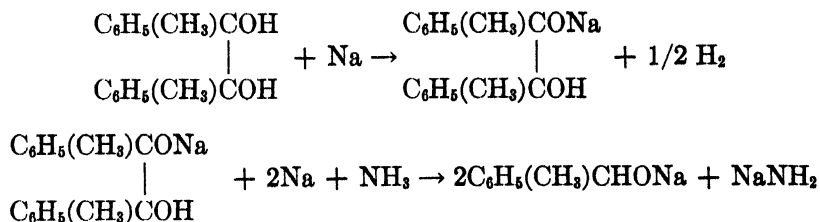
TABLE 11—*Concluded*

ALCOHOL	SALT FORMED	REFERENCES	NOTES
Naphthols (and tetrahydronaphthols)			
$\alpha$ -Naphthol:			
$C_{10}H_7OH$ . . . . .	$C_{10}H_7ONa$	379	
	$C_{10}H_{11}ONa$ <i>ar</i>	379	
$\beta$ -Naphthol:			
$C_{10}H_7OH$ . . . . .	$C_{10}H_{11}ONa$ <i>ac</i>	379	
	$C_{10}H_{11}ONa$ <i>ar</i>	379	

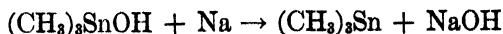
to the tetrahydronaphthols, so that the preparation of the pure naphthoxides requires the use of an alkali amide rather than the free metal.

The salts of alcohols, phenols, and naphthols which have been prepared by reaction with solutions of the alkali and alkaline-earth metals are assembled, together with references, in table 11. The alkali salts of this type have been utilized for the preparation of ethers (interaction with alkyl halides) (52, 240, 361, 379) and of lead and thallium (ous) alkoxides (metathesis between soluble alkoxides and soluble salts of lead and thallium) (50, 52, 58).

Sodium in liquid ammonia replaces only one of the hydrogen atoms of pinacol; it reacts extensively with acetophenone pinacol, first to replace one hydrogen and then to cleave a carbon-carbon bond (392),



Trimethylstannyl hydroxide reacts with sodium in liquid ammonia as follows (121):



The complex hydroxybromide,  $[(CH_3)_3SnOH]_2 \cdot (CH_3)_3SnBr$ , reacts in somewhat the same manner. At first trimethylstannyl precipitates, and then it goes into solution as more sodium is added to form sodium trimethylstannide,  $NaSn(CH_3)_3$ . As the reaction proceeds, gelatinous sodium hydroxide precipitates (197).



## V. ETHERS AND OXIDES

The simple ethers, both aliphatic and aromatic,<sup>8</sup> are not acted upon by solutions of metals in liquid ammonia (242). Indeed, diethyl ether has been advantageously used as a diluent for carrying out liquid ammonia-metal reductions (70, 359, 400). When, however, the hydrocarbon portion of an ether contains a substituent normally reactive toward solutions of metals, reaction does occur. Thus, with sodium in liquid ammonia  $\beta$ -bromoethyl phenyl ether gives 1,4-diphenoxybutane and phenol, while  $\gamma$ -bromopropyl phenyl ether gives phenoxypropane, phenol, and 1,6-diphenoxyhexane (69).

While the bond between oxygen and carbon resists the action of metal solutions, the bonds between oxygen and such elements as germanium and tin are broken by the action of a solution of sodium. Thus triphenyl-germanium oxide reacts with sodium to form sodium triphenylgermanide and sodium triphenylgermanolate (254),



Triethylgermanium oxide reacts similarly with lithium in ethylamine (204). Sodium in liquid ammonia converts trimethylstannyl phenoxide,  $(CH_3)_3SnOC_6H_5$ , into sodium phenoxide and either trimethylstannyl or sodium trimethylstannide, depending upon the quantity of sodium used (222).

## VI. AMINES

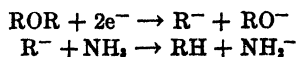
A few of the simple aliphatic amines dissolve some of the alkali metals (see part I, section II) and react with the dissolved metal to form substituted metal amides:  $CH_3NHCs$  (319),  $C_2H_5NHCs$ , and *iso*- $C_4H_9NHCs$  (318). Usually, however, such reactions do not take place readily except at elevated temperatures (79), and most amines may be safely stored over sodium to insure complete dehydration.

Liquid ammonia is not a suitable medium for the preparation of salts of the aliphatic amines, since such substances are extensively ammonolyzed (318),

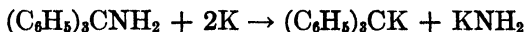


Tributylamine has been recommended as a diluent to increase the solubility of certain organic halogen compounds in the liquid ammonia-sodium

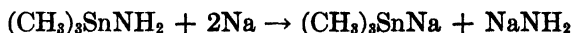
<sup>8</sup>Since submitting this paper for publication, an important article (328a) has appeared which clearly demonstrates that diphenyl ether as well as its ortho and para mono- and di-substitution products are cleaved rapidly and quantitatively at the carbon-oxygen linkage by sodium in liquid ammonia,



method of analysis for halogens (359). The monosodium salts of aniline, ethylaniline, *o*-toluidine, and diphenylamine have been formed by treating the amine with sodium in liquid ammonia in an autoclave at room temperature. These reactions did not occur readily at  $-40^{\circ}\text{C}$ . Disodium anilide and sodium benzylamide could not be formed (312). Sodium diphenylamide has been prepared by the interaction of sodium and diphenylamine at  $-33^{\circ}\text{C}$ . (168, 377). Sodium and potassium react with triphenylmethylaniline to form an alkali triphenylmethide and the corresponding amide (233),



Trimethylstannylamine reacts similarly with sodium in ammonia (223),



#### VII. ALDEHYDES AND RELATED COMPOUNDS

Since the aldehydes are themselves reactive toward liquid ammonia, this medium is suitable only for reactions between aldehyde derivatives and solutions of metals. Acetaldehyde ammonia and sodium react ( $-33^{\circ}\text{C}$ .) in the ratio of one mole of the former to one gram-atom of the latter to give one equivalent of hydrogen and a precipitate which was taken to be  $\text{CH}_3\text{CH}(\text{ONa})\text{NH}_2$  (242). Aldehyde ammonia, however, appears to be a hydrate of triethylidene triimine,  $(\text{CH}_3\text{CH}:\text{NH})_3 \cdot 3\text{H}_2\text{O}$  (353), so that the precipitate might well have been sodium hydroxide. Similarly, benzaldehyde reacts with liquid ammonia to form a precipitate which is acted upon by sodium (244).

The acetals are not very reactive toward liquid ammonia and are seemingly stable toward solutions of metals, since dimethylacetal has been recommended as a diluent in the liquid ammonia-sodium method of analysis for organic halogens (359).

Hexamethylenetetramine,  $(\text{CH}_2)_6\text{N}_4$ , and *N, N, N, N*-tetramethylmethylenediamine,  $[(\text{CH}_3)_2\text{N}]_2\text{CH}_2$ , are not acted upon by sodium in liquid ammonia. *N*-Ethylideneethylamine,  $\text{CH}_3\text{CH}:\text{NC}_2\text{H}_5$ , forms *N, N*-diethyl-2,3-butanediamine,  $\text{CH}_3\text{CH}(\text{NHC}_2\text{H}_5)\text{CH}(\text{NHC}_2\text{H}_5)\text{CH}_3$ , when treated with a sodium solution in an autoclave at room temperature. This reaction does not occur at  $-40^{\circ}\text{C}$ . and is incomplete at  $-20^{\circ}\text{C}$ . (311). Benzylideneimine,  $\text{C}_6\text{H}_5\text{CH}:\text{NH}$ , is reduced to benzylamine by sodium in liquid ammonia (351).

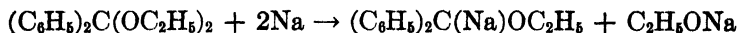
#### VIII. KETONES AND RELATED COMPOUNDS

The reactions of only a few ketones with solutions of metals have been studied. One mole of acetone reacts with one gram-equivalent of sodium without the formation of any gas, but the reaction product has not been

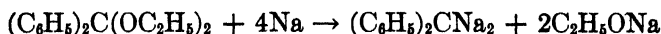
definitely characterized (244). Benzophenone in ammonia solution reacts with one equivalent of sodium to form a monosodium ketyl,  $(C_6H_5)_2CONa$ , and with two equivalents to form a disodium ketyl,  $(C_6H_5)_2CNaONa$  (190, 244, 331, 386, 387). A salt of the composition  $C_7H_5O_2K$  has been obtained by the action of a potassium solution on dimethylpyrone (331).

The reduction of two chlorine-substituted ketones has been studied, but the results are not entirely conclusive.  $\alpha$ -Chloroacetophenone reacts in liquid ammonia with 2.2 atoms of sodium to give a nitrogen- and chlorine-free reddish oil (45 per cent by weight of original ketone) from which acetophenone (13 per cent), a colorless solid (1.3 per cent), and tar may be obtained.  $\beta$ -Chloropropiophenone similarly reacts with 1.53 atoms of sodium to give a nitrogen- and chlorine-free viscous oil (68.8 per cent), which solidifies to a hard resin (69).

Benzophenone diethylketal reacts with sodium and potassium solutions ( $-33^\circ C.$ ) to form sodium and potassium ethoxydiphenylmethides and the corresponding ethoxides (391),



At the same time about 14.4 per cent of the acetal is doubly cleaved,



By the action of one gram-atom of potassium in liquid ammonia upon one mole of benzil, one obtains a solution colored a deep blue-violet and, by the action of two gram-atoms of potassium, a deep red solution and precipitate. Neither the monopotassium nor the dipotassium salt is pure, because even at low temperatures benzil reacts with ammonia to form high-melting, nitrogen-containing products (350).

Solutions of metallic potassium and sodium in liquid ammonia give with benzophenoneimine,  $(C_6H_5)_2C:NH$ , highly colored (red) and very soluble products, which cannot be freed from ammonia, and an excess of-metal for analysis. In each case, however, there is reduction (up to 50 per cent) to benzohydrylamine or the product of its reaction with benzophenoneimine, benzophenonebenzohydrylamine. Other facts concerning the reaction indicate that this reduction takes place through the formation of the monosodium ketyl of benzophenoneimine, followed by ammonolysis to an equimolecular mixture of amine and imine together with sodium amide. Some disodium ketyl may be formed, but the amount is very small (346).

#### IX. CARBOHYDRATES

Schmid and coworkers (334, 338) have studied the reaction of carbohydrates with solutions of sodium and potassium in liquid ammonia, and report the rapid formation of monoalkali salts of glucose, fructose,  $\alpha$ -

methylglucoside, glycogen, inulin, soluble starch, lichenin, and chitin. With excess of alkali metal further reaction is slow and proceeds in a different manner, since the products obtained contain nitrogen.

As intermediates in the synthesis of carbohydrate derivatives, Muskat and others (136, 274, 298, 299) have prepared ( $-33^{\circ}\text{C}.$ ) a number of potassium salts of carbohydrates (not isolated): tetrapotassium  $\alpha$ -methylmannoside, tripotassium monoacetoneglucose, monopotassium diacetoneglucose, monopotassium acetone methylrhamnoside ( $\gamma$ ), monopotassium 2,3-acetonemethylrhamnopyranoside, octapotassium sucrose (?), and monopotassium heptamethylisoscrose. Sugars with potential aldehyde or ketone groups react with liquid ammonia to form the corresponding amines. Methylation of fructose methylphenylosazone by the method of Muskat (alkali metal salt + methyl iodide) led to cleavage of the N-N linkages instead of methylation of the hydroxyl groups. The only crystalline product isolated was trimethylphenylammonium iodide (78). This technique of methylation has been applied to acetylstarch and to the Schardinger dextrans (104a).

Cellulose reacts rapidly with an ammonia solution of sodium to form the monosodium derivative. This product is in turn slowly converted into the trisodium derivative  $[\text{C}_6\text{H}_7\text{O}_2(\text{ONa})_3]_x$ , which is stable toward an excess of the metal (330, 339).

## X. ACIDS AND THEIR DERIVATIVES

### A. Simple carboxylic acids

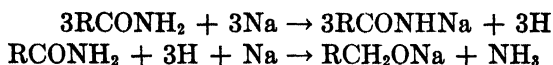
In liquid ammonia the carboxylic acids react to form ammonium salts. The reactions of ammonium salts have already been treated in section II of part I. While sodium acetate is inactive toward sodium in ammonia, sodium benzoate does react, although the resulting products have not been determined (245, 328a).

### B. Acid amides, amidines, cyanamide, and dicyanodiamide

The acid amides react as monobasic acids with solutions of the alkali metals to liberate hydrogen and form salts. Sodium and potassium acetamide,  $\text{CH}_3\text{CONHK}$ , have been prepared in this manner (100), as well as the sodium salts of benzenesulfonamide, succinimide, benzoic sulfimide, and urea (99). Sodium in excess of one atom reacts slowly and incompletely with a very dilute solution of urea in liquid ammonia ( $-33^{\circ}\text{C}.$ ). Apparently the product is a mixture of mono- and di-sodium urea (137). Magnesium reacts similarly with acetamide,  $(\text{CH}_3\text{CONH})_2\text{Mg}\cdot 4\text{NH}_3$  (99, 101), benzenesulfonamide,  $(\text{C}_6\text{H}_5\text{SO}_2\text{NH})_2\text{Mg}\cdot n\text{NH}_3$ , (102), succinimide, benzoic sulfimide, urea (99), and cyanamide (102). Calcium and mag-

nesium form with dicyanodiamide the following salts:  $\text{Ca}(\text{H}_3\text{C}_2\text{N}_4)_2 \cdot 4\text{NH}_3$  and  $\text{Mg}(\text{H}_3\text{C}_2\text{N}_4)_2 \cdot 2\text{NH}_3$  (94).

In studying the reactions of acid amides with sodium in liquid ammonia ( $-50^\circ\text{C}.$ ), Chablay (51, 59) observed not only the formation of sodium salts but also the reduction of a part of the amide to the corresponding alcohol:



Acetamide, propionamide, butyramide, and isovaleramide react rapidly, while capronamide, caprylamide, and higher homologues react very slowly.

Diphenylmethylformamidine,  $\text{C}_6\text{H}_5\text{N}:\text{CH}\cdot\text{N}(\text{CH}_3)\text{C}_6\text{H}_5$ , reacts with sodium in ammonia (room temperature) to form a sodium salt (384).

### C. Amino acids and proteins

Voss and Gutterman (369) prepared (low temperatures) the sodium salts of the following amino acids: glycine,  $\text{CH}_2(\text{NH}_2)\text{CO}_2\text{Na}$ , *dl*-alanine,  $\text{CH}_3\text{CH}(\text{NH}_2)\text{CO}_2\text{Na}$ , *dl*-leucine,  $(\text{CH}_3)_2\text{CHCH}_2\text{CH}(\text{NH}_2)\text{CO}_2\text{Na}$ , *dl*-phenylalanine,  $\text{C}_6\text{H}_5\text{CH}_2\text{CH}(\text{NH}_2)\text{CO}_2\text{Na}$ , sarcosine,  $\text{CH}_3\text{NHCH}_2\text{CO}_2\text{Na}$ , *l*-tyrosine, *p*- $\text{NaOC}_6\text{H}_4\text{CH}_2\text{CH}(\text{NH}_2)\text{CO}_2\text{Na}$ ,  $\beta$ -alanine,  $\gamma$ -amino-*n*-butyric acid,  $\text{H}_2\text{N}(\text{CH}_2)_3\text{CO}_2\text{Na}$ , and *d*-glutamic acid,  $\text{NaO}_2\text{CCH}_2\text{CH}_2\text{CH}(\text{NH}_2)\text{CO}_2\text{Na}$ .

Miller and coworkers (280, 288, 289, 325) have examined the reactions of solutions of sodium in liquid ammonia ( $-33^\circ\text{C}.$ ) with amino acids, proteins, and related substances. Table 12 gives the ratio of the moles of hydrogen evolved to the moles of substance used when the various substances and mixtures are treated with a slight excess of sodium. Table 13 gives the ratio of the moles of hydrogen evolved to the moles of diketopiperazine used when various amounts of sodium are added. These results lead to the following conclusions: (1) Glycine and alanine react as monobasic acids. (2) The phenolic hydroxyl group of tyrosine is slightly acidic. (3) Some tyrosine seems to be reduced in the treatment. (4) Leucine liberates more hydrogen than does a monoaminomonocarboxylic acid. (5) Cystine is reduced by sodium acting directly on the disulfide bond (see below). (6) The peptide linkage in dipeptides is not acidic in liquid ammonia. (7) Diketopiperazine is reduced by sodium in liquid ammonia. (8) Mixtures of amino acids and of diketopiperazine do not liberate hydrogen, additively, as is to be expected (289). Proteins (silk fibroin, casein, edestin, and silk) are acidic in liquid ammonia and react readily with sodium and potassium to form hydrogen and ammonolytic products containing alkali metal. The reaction of glycyl-*dl*-alanine shows that the imide link of the peptide is not quantitatively reduced by sodium

in liquid ammonia. Glycine ethyl ester hydrochloride similarly treated yielded some of the glycine ester and an unidentified product, while *N*-methylacetamide was not completely reduced or decomposed (280). In general, the reactions of proteins with sodium in liquid ammonia occur more slowly than do similar reactions involving amino acids or dipeptides, and are sometimes complicated by the catalytic activity of the proteins

TABLE 12

*Reaction of amino acids and related substances with sodium in liquid ammonia*

SUBSTANCE	MOLES OF H <sub>2</sub> /MOLES OF SUBSTANCE	
Glycine . . . . .	0 50	
Alanine . . . . .	0 48	0 48
Tyrosine . . . . .	0 65	0 67
Glycolic acid . . . . .	0 94	0 96
<i>l</i> -Cystine . . . . .	0 53	0 55
<i>l</i> -Leucine . . . . .	0 64	
Diketopiperazine . . . . .	0 32	
Glycylglycine . . . . .	0 51	
Glycyl- <i>dl</i> -alanine . . . . .	0 51	0 52
<i>N</i> -Methylacetamide . . . . .	0 53	0 54
Acetanilide . . . . .	0 05	0 06
Glycylglycine and diketopiperazine, mole ratio 1:1 . . . . .	0 02	0 02
Glycylglycine, 2 moles, and diketopiperazine, 1 mole. . . . .	0 05	0 05
Glycine and tyrosine, mole ratio 1:1 . . . . .	0 39	
Glycine 53.3 per cent, alanine 31.1 per cent, tyrosine 15.6 per cent. .	0 36	

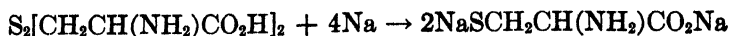
TABLE 13

*Action of sodium in liquid ammonia upon diketopiperazine*

SUBSTANCE	ATOMIC WEIGHTS OF Na	MOLES OF H <sub>2</sub> /MOLES OF SUBSTANCE
	MOLES OF SUBSTANCE	
Diketopiperazine . . . . .	0 50	0 04
	1 00	0 06
	2 00	0 32
	3 00	0 32
	4 00	0 32

(notably hemoglobin and hematin) toward the reaction between sodium and ammonia (326). Parathyroid hormone behaves as a typical protein toward sodium and is apparently without catalytic activity (327).

Cystine has been shown to be reduced to cysteine by sodium in liquid ammonia (362, 366, 368),





Benzyl ester of $\beta$ -(benzylmercapto)- $N$ -( $N^{\alpha}$ -carbobenzoxyl-glutamyl)alanine $\text{CH}_3\text{CH}_2\text{CONH}_2$ $\text{CHNHOCOC}_6\text{H}_5$ $\text{CONHCHCO}_2\text{C}_6\text{H}_5$ $\text{CH}_2\text{SC}_6\text{H}_5$	$N$ -glutaminylcysteine $\text{CH}_3\text{CH}_2\text{CONH}_2$ $\text{CHNH}_2$ $\text{CONHCHCO}_2\text{H}$ $\text{CH}_2\text{SH}$ (60 per cent)	122
Homocysteine, $\text{S}_1[\text{CH}_2\text{CH}_2\text{CH}(\text{NH}_2)\text{CO}_2\text{H}]_2$	Na salt of homocysteine, $\text{NaSCH}_2\text{CH}_2\text{CH}(\text{NH}_2)\text{CO}_2\text{Na}$	39, 363, 366, 367
$S$ -Benzyl- $N$ -methylhomocysteine	Na salt of cysteine	303a
$S$ -Benzylcysteine	Na salt of cysteine	345
$S$ -Benzyl- $L$ -cysteine	Na salt of $L$ -cysteine	367
$S$ -Benzyl- $dl$ -homocysteine	Na salt of homocysteine	324, 367
$S$ -Benzyl- $d$ -homocysteine	Bibenzyl, some toluene	304
$S$ -Benzyl- $L$ -homocysteine	Sodium $d$ -cysteinate	367
$S$ -Benzyl- $L$ -homocysteine	Sodium $L$ -cysteinate	367
Pentocysteine	Sodium pentocysteinate	364
$L$ -Histidine	Sodium salt	362a
$p$ -Toluenesulfonyl- $N$ -methyl-1(or 3)-benzyl- $L$ -histidine	$L$ -Amino- $N$ -methylhistidine	362a



Some sodium sulfide and alanine seem also to be formed in the reduction of cystine (107).

In connection with synthetic studies in the field of the amino acids and their derivatives, du Vigneaud and others have examined the conduct of a number of substances toward liquid ammonia solutions of sodium ( $-33^{\circ}$  to  $-77^{\circ}\text{C}.$ ). The results of these investigations are given in table 14. The sodium solution is a particularly valuable reagent in this field. In none of the reductions studied was racemization encountered. Hence optically active derivatives of active substances may be prepared readily by

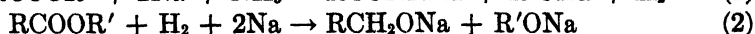
TABLE 15  
*Reduction of esters by sodium in liquid ammonia*

ESTER REDUCED	ALCOHOLS OBTAINED
<b>Esters of monocarboxylic acids:</b>	
Methyl <i>n</i> -butyrate.....	Butanol
Methyl isovalerate. . . . .	Isoamyl alcohol
Ethyl caproate.....	Hexanol
Methyl heptylate.....	Heptanol
Methyl caprylate..	Octanol
Methyl laurate.....	Dodecanol ( $\text{C}_{12}\text{H}_{25}\text{OH}$ )
Methyl myristate.....	Tetradecanol ( $\text{C}_{14}\text{H}_{29}\text{OH}$ )
Methyl palmitate.....	Hexadecanol ( $\text{C}_{16}\text{H}_{33}\text{OH}$ )
<b>Esters of dicarboxylic acids:</b>	
Methyl sebacate, $\text{CH}_3\text{O}_2\text{C}(\text{CH}_2)_8\text{CO}_2\text{CH}_3$ . . . . .	Decanediol-1,10
Dimethyl $\alpha$ , $\alpha'$ -dimethylglutarate, $\text{CH}_3\text{O}_2\text{CC}(\text{CH}_3)_2(\text{CH}_2)_2\text{CO}_2\text{CH}_3$ ..	2,2-Dimethylpentanediol-1,5
<b>Esters containing an aromatic radical:</b>	
Ethyl phenylacetate, $\text{C}_6\text{H}_5\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ . . . . .	Phenylethyl alcohol, $\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{OH}$
Methyl cinnamate, $\text{C}_6\text{H}_5\text{CH:CHCO}_2\text{CH}_3$ .....	Phenylpropyl alcohol, $\text{C}_6\text{H}_5(\text{CH}_2)_2\text{CH}_2\text{OH}$

methylation or by hydrolysis (plus oxidation) of the intermediate sodium salts.

#### *D. Esters*

When esters of carboxylic acids are treated with sodium in liquid ammonia ( $-50^{\circ}\text{C}.$ ), two reactions occur,



These reactions were observed using the following esters: ethyl acetate, methyl butyrate, methyl isovalerate, ethyl caproate, and methyl caprylate

(51, 60). Esters dissolved in absolute alcohol and added to sodium solutions ( $-80^{\circ}\text{C}.$ ) are reduced in the following manner:



Esters so treated and the alcohols obtained are given in table 15. Methyl cinnamate did not give the expected cinnamic alcohol,  $\text{C}_6\text{H}_5\text{CH}:\text{CHCH}_2\text{OH}$ , but rather phenylpropyl alcohol, owing to the hydrogenation of the double bond (53).

### *E. Nitriles*

Sodium in liquid ammonia reacts vigorously with  $\alpha$ -tolunitrile to form a sodium salt,



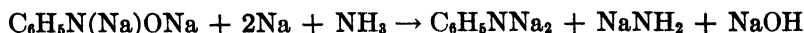
which, when treated with alkyl halides, reacts to form  $\alpha$ -alkyl- $\alpha$ -tolunitriles. Some toluene (and presumably sodium cyanide) accompanies the formation of the sodium salt (3). Benzonitrile reacts rapidly with two atoms of sodium to give a wine-red solution and a white precipitate. The reaction products have not been determined, although only traces of cyanide are present (250).

### XI. ORGANIC NITRO AND AZOXY COMPOUNDS. DERIVATIVES OF HYDRAZINE, HYDROXYLAMINE, AND DIIMIDE

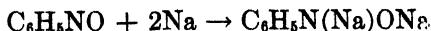
White and Knight (378) have studied the products of reduction of nitrobenzene and related compounds with solutions of metals in liquid ammonia. Nitrobenzene yields with both sodium and potassium the dialkali phenylhydroxylamine according to the equation,



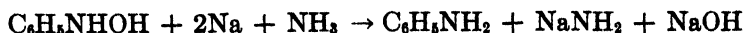
An excess of sodium completely reduced the nitrogen atom, probably to disodium anilide,



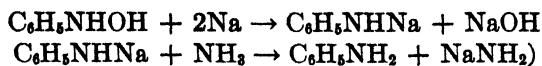
When water is added to partially reduced nitrobenzene and liquid ammonia, azoxybenzene and azobenzene result from the familiar reactions of phenylhydroxylamine in alkaline aqueous solution. Nitrosobenzene with sodium or potassium produces dialkali phenylhydroxylamine,



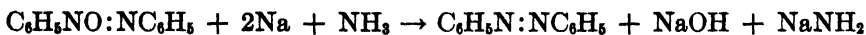
while phenylhydroxylamine itself is reduced directly to aniline by two atoms of sodium without the liberation of hydrogen,



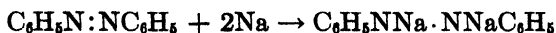
(Perhaps the latter reaction proceeds thus,



Azoxybenzene is reduced to azobenzene,



and the latter to the disodium salt of hydrazobenzene,



The statement of White and Knight that the N-N bond in disodium benzhydrazide is ruptured by an excess of sodium has been disproved by Kraus and Bien (190).

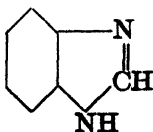
Hydrazotriphenylmethane and hydrazophenylfluorene [*s*-bis(9-phenyl-9-fluoryl)hydrazine],  $\text{C}_6\text{H}_5\text{C}_{13}\text{H}_8\text{NHNHC}_{13}\text{H}_8\text{C}_6\text{H}_5$ , react vigorously with sodium in liquid ammonia at 0°C. to form products (probably sodium salts) which, upon treatment with water, yield triphenylmethane (90 per cent) and 9-phenylfluorene,  $\text{C}_6\text{H}_5\text{C}_{13}\text{H}_9$ , respectively (313).

## XII. HETEROCYCLIC NITROGEN RING SYSTEMS

### A. Five-membered rings

Franklin (93) has examined the reactions of metals with pyrrole, indole, and carbazole. Pyrrole discharges the blue color of a solution of potassium in liquid ammonia with the evolution of hydrogen, but the potassium salt so formed could not be brought to crystallization. Calcium and magnesium react similarly, and the solubility of the salts is such as to permit their isolation:  $(\text{C}_4\text{H}_4\text{N})_2\text{Ca} \cdot 4\text{NH}_3$  and  $(\text{C}_4\text{H}_4\text{N})_2\text{Mg} \cdot 2\text{NH}_3$ . That there is little reduction of the pyrrole to tetrahydropyrrole is attested by the fact that 91.6 per cent of the theoretical amount of hydrogen was obtained from one reaction with calcium. The calcium and magnesium salts,  $(\text{C}_8\text{H}_6\text{N})_2\text{M} \cdot 4\text{NH}_3$ , of indole may be prepared similarly. The failure to obtain much more than half of the expected amount of hydrogen from the reaction with calcium indicates that extensive reduction to dihydroindole accompanies these reactions. With carbazole and potassium reduction is so extensive that only a very small amount of hydrogen is liberated and the solution becomes strongly colored.

Imidazole,  $\text{HN}-\text{CH}:\text{N}-\text{CH}:\text{CH}$ , and magnesium react in liquid ammonia to form a magnesium salt,  $(\text{C}_3\text{H}_3\text{N}_2)_2\text{Mg}$ , and hydrogen (373). Benzimidazole,



forms a monosodium salt and 0.92 equivalent of hydrogen by a similar reaction (385). The calcium and magnesium salts of lophine (2,4,5-triphenylimidazole) and 1,2,4-triazole,  $\text{HN}-\text{CH:N}-\text{CH:N}$ , and the calcium salt of tetrazole,  $\text{HN}-\text{N:N}-\text{CH:N}$ , are prepared in the same manner (352).

### B. Six-membered rings

Pyridine and sodium in liquid ammonia (both at  $-60^\circ\text{C}$ . and at room temperature) form a substance,  $(\text{C}_5\text{H}_5\text{NNa})_2\cdot\text{NH}_3$ , which reacts with various alkyl halides to form non-crystallizable, ether-soluble, basic products and yields a hydrate of tetrahydrodipyrindyl,  $(\text{C}_5\text{H}_5\text{N})_2\cdot\text{H}_2\text{O}$ , upon decomposition with 95 per cent alcohol and small quantities of water in the presence of ether (272).

### XIII. ORGANIC COMPOUNDS OF SULFUR

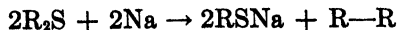
The reducing action of sodium in liquid ammonia upon certain organic sulfur compounds has been utilized for the analytical determination of sulfur in these substances. Sodium sulfide and sulfite so formed are then oxidized by sodium peroxide and precipitated as barium sulfate. This method has been found to be satisfactory for the following compounds: thiourea, benzoyl sulfimide, acetone diethyl sulfone, diphenyl sulfone, dinitrophenyl thiocyanate, benzenesulfonamide, benzenesulfonyl chloride, *n*-propyl *p*-toluenesulfonate, *p*-toluenesulfonic acid, and 2-naphthylamine-5,7-disulfonic acid (348).

Alkyl mercaptans (211, 380) and phenyl mercaptan (211, 242, 379) react with liquid ammonia to form ammonium salts,  $\text{RSNH}_4$ , which in turn react with sodium to form the corresponding sodium mercaptides.

Aliphatic sulfides (ethyl, *n*-propyl, and *n*-heptyl) react with sodium in liquid ammonia chiefly according to the equation,



although the high ratio of sodium ethylmercaptide to sodium amide indicates some such concomitant reaction as (380)



Diphenyl sulfide, while reacting with sodium in the same mole ratio, furnishes benzene, sodium sulfide, and a small amount of a water-insoluble gas (250). A particularly interesting reduction of a sulfide is that of (12-phenyl-12- $\beta$ -benzoxanthylmercapto)acetic acid, which with sodium in liquid ammonia forms a deep orange-brown sodium triarylmethyl. After reaction with a slight excess of ammonium bromide, the resulting colorless

trisubstituted methane is found to be optically active, showing that the sodium salt (or ion) must also be active (1).

When treated with sodium in liquid ammonia, aliphatic disulfides (ethyl, *n*-propyl, and isoamyl) are reduced quantitatively to the corresponding mercaptides (380),



Advantage has been taken of the reactivity of ammonia solutions of metals (sodium, potassium, calcium, and barium) toward sulfur compounds in the purification of petroleum oil (64).

From the reaction products of sodium upon phenyl isothiocyanate,  $C_6H_5NCS$ , aniline, sodium sulfide (no cyanide), and a little biphenyl have been isolated. Sodium benzenesulfonate reacts with two atoms of sodium to furnish benzene (71 per cent), sodium sulfite, and a small amount of biphenyl (250).

The amidosulfonic acid derived from vitamin  $B_1$  reacts with sodium in liquid ammonia to form low yields of 2,5-dimethyl-6-aminopyrimidine (65a, 381). For the reactions of benzenesulfonamide and benzoic sulfimide see section X, B; for those of amino acids containing sulfur see section X, C.

The authors take this opportunity to acknowledge their great indebtedness to Mr. W. R. Stemen of the editorial staff of *Chemical Abstracts* for his many helpful suggestions, particularly with respect to the nomenclature of organic compounds. The reader of future years may supplement this summary of reactions of solutions of metals by consulting the annual reviews of liquid ammonia research which appear in *The Journal of Chemical Education*.

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# THE HYDROGEN BOND AND ASSOCIATION<sup>1</sup>

EDWIN N. LASSETTRE

*Gates and Crellin Laboratories of Chemistry, California Institute of Technology,  
Pasadena, California*

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## I. INTRODUCTION

The phenomenon of association was known to chemists at a very early date, but its wide-spread character became most evident in the latter part of the nineteenth century through the extensive investigations of molecular weights in solution. In 1891 Nernst (28) made an important contribution to the field by successfully accounting for the distribution of

<sup>1</sup> Contribution No. 585.



benzoic acid between water and benzene, assuming doubled molecules in the benzene phase.

At first it was supposed that organic compounds are polymerized only when they contain hydroxyl groups, but this was disproved by Auwers (2), who showed that the anilides are polymerized in most cases. Auwers also showed that the ortho-substituted phenols are less likely to be polymerized than the meta and para compounds, and the much later work of Sidgwick (39) showed that other properties also of ortho-substituted compounds may be strikingly different from those of the meta and para compounds.

Latimer and Rodebush in 1920 (25) proposed a theory which correlated and explained many of these facts and which is now generally accepted. The proposal of Latimer and Rodebush was that, under suitable conditions, a proton can form a bond between two atoms. Such a bond is customarily called a hydrogen bond.

Newer methods of investigation have provided extensive experimental material which in general confirms the theory in a remarkable manner. The investigation of crystal structures of both inorganic and organic compounds has revealed several structures which can be explained from the hydrogen bond point of view. One of the most important contributions was made by Pauling and Brockway (29), whose electron diffraction investigation of formic acid led to the determination of the structure of the dimer and thus opened the way to a better understanding of the polymerization of the organic acids; similar results have been provided by the crystal structure studies of oxalic acid and other carboxylic acids. Another recent and very important contribution to our knowledge of both the existence and properties of hydrogen bonds has been made by Wulf and collaborators (20, 42), who investigated the infra-red absorption spectra of many organic compounds in solution and were able to interpret the spectra in terms of hydrogen-bond formation.

In the present paper the older data, relating particularly to molecular weights and distribution ratios, are reviewed and correlated with the newer theories whenever possible. No attempt is made to include the results of crystal structure, electron diffraction, or absorption spectra investigations, but the deductions from classical data are compared with these results whenever possible and the concepts which have arisen from these investigations are freely used. For purposes of continuity in presentation the results are not necessarily presented in chronological order.

## II. MOLECULAR WEIGHTS. GENERAL CONSIDERATIONS

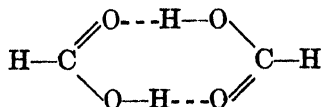
The three most important classical methods of determining molecular weights involve the measurement of vapor density, freezing-point lowering,

and boiling-point raising. For the sake of clarity a brief discussion of the freezing-point equation will be given. This equation depends upon the validity of Raoult's law and upon the assumptions of perfect gases. The assumption that the solid phase is *pure solvent* is very important; the formation of solid solutions completely invalidates this equation. The presence of a solid solution would make the freezing-point lowering less than expected and might be interpreted as polymerization. The studies of freezing-point lowering with which we shall be concerned were not accompanied by an investigation of the solid phase, but it is thought that solid solutions do not often occur in these cases. The possibility of deviations from the laws of perfect solutions due to causes other than polymerization is dealt with empirically by giving as a standard the molecular weight determination of a normal compound for each solvent concerned if possible.

### III. THE ENERGY OF THE HYDROGEN BOND FROM VAPOR DENSITY AND DISTRIBUTION DATA

The heats of dissociation of polymers held together by hydrogen bonds can be obtained in a few cases from data on the change in equilibrium constant with temperature, determined by measurement of vapor density or of distribution ratio. The vapor densities of three organic acids have been carefully studied. The vapor densities of formic or acetic acid could be consistently interpreted in terms of a dimer in equilibrium with a monomer, and from the measurements values of the dissociation energy were obtained. Two other reactions, the polymerizations of benzoic and salicylic acids, have been studied in solution by investigating the change with both temperature and concentration of the distribution ratio between two immiscible solvents. These latter results are highly uncertain, but are apparently the only ones available for reactions in solution.<sup>2</sup>

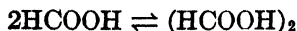
One of the most investigated polymers is the dimer of formic acid. The electron diffraction investigation of Pauling and Brockway (29) has shown that the dimer has the structure



where the broken lines indicate hydrogen bonds. The geometry of this configuration is such that the hydrogen lies on the straight line joining the two oxygens, and the two carboxyl groups lie in the same plane. This

<sup>2</sup> A more complete discussion of bond energies is to be found in a paper by Huggins (J. Org. Chem. 1, 407 (1936)).

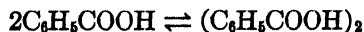
structure involves two hydrogen bonds, as shown. The heat of dissociation of formic acid divided by 2 should be approximately the hydrogen bond energy. The reaction



has been the subject of a very careful study by Coolidge (15), who found the heat of dissociation of formic acid to be 14,125 cal. per mole, corresponding to the value 7063 cal. per mole for the energy of the hydrogen bond.

The vapor density of acetic acid has been studied by Fenton and Garner (16), who obtained 14,900 cal. per mole as the heat of dissociation. The vapor density of acetic acid has also been studied by MacDougall (26), who found 16,400 cal. per mole for the heat of dissociation. The latter result is probably more reliable than the former, since the study was made at such low pressures that the perfect gas laws are valid. If MacDougall's value is adopted, the bond energy is 8200 cal. per mole, assuming the same structure as for formic acid. This value is not in particularly good agreement with that obtained from formic acid and indicates that the introduction of substituents considerably changes the bond energy. Hexoic acid was also studied by Fenton and Garner, but no consistent results were obtained.

All the above values are for the gaseous materials, and it is desirable to have a value for reactions in solution. A study of the distribution of benzoic acid between two phases was made by Hendrixson (21) long ago. The distribution experiments were interpreted by assuming that the benzoic acid in the organic phase is partially polymerized into a double molecule and in water exists entirely as single molecules. It was possible to interpret the data with an equilibrium constant of the reaction



and a distribution constant. By performing experiments at various temperatures the heat of dissociation was obtained. With benzene as the organic phase the heat of dissociation was found to be 8710 cal. per mole, and with chloroform 8350 cal. per mole. From these data the apparent hydrogen bond energies are found to be 4400 and 4200 cal. per mole, respectively. These measurements are subject to a serious uncertainty due to the transfer of water into the organic liquid layer by hydration of the acid.

Salicylic acid was also studied by Hendrixson (21), the solvents being again benzene and chloroform. The heats of dissociation obtained were 5630 cal. per mole and 7680 cal. per mole, respectively. The values will not be interpreted in terms of bond energies, because the presence of the hydroxyl group in the ortho-position makes such an interpretation uncer-

tain. The fact that these energies are lower than those for benzoic acid may be due to the presence of the hydroxyl group or to the fact that an increase in hydration occurs which invalidates the results. That hydration is not a negligible factor is shown by the work of E. Cohen and collaborators (14, 13) and also by Szyszkowski (41), who investigated the solubility of benzoic acid in dry benzene and in benzene containing varying amounts of water. It was found that the solubility in benzene is increased by the presence of water. The solubility of benzoic acid in benzene at 25°C. was found to be about 3 per cent lower than that in benzene saturated with water, while the solubility of salicylic acid was about 30 per cent lower. This suggests that the distribution experiments on benzoic acid are approximately right, while those for salicylic acid are likely to be considerably in error. Other data bearing on this subject are presented in a following section.

#### IV. THE QUALITATIVE INTERPRETATION OF EXPERIMENTS ON THE LOWERING OF THE FREEZING POINT IN TERMS OF POLYMERIZATION

The ease of reversal of reactions involving hydrogen bonds precludes the study of polymers by actual isolation and subsequent study of their properties. The properties of the polymers are obtained by inference from the study of complicated mixtures of polymers of all orders. The properties of greatest interest in the study of a given compound, or compounds, are the arrangements of the atoms in space, or structure, and the rate and equilibrium of the reactions which the compound undergoes with other compounds. A consideration of molecular weights obtained by the classical methods might well provide information concerning the equilibrium constants of certain reactions involving the polymers, but can provide information concerning the structure of polymers only by inference, if at all. Nevertheless certain reasonable conclusions concerning structure can be drawn by considering molecular weights, provided we keep in mind the large accumulation of experimental evidence on internuclear distances resulting from studies of x-ray and electron diffraction by various compounds. This will be illustrated by the qualitative considerations of the remainder of this section, and data will be given which indicate the general properties to be expected of compounds which can form hydrogen bonds.

It is found, in general, that the molecular weights of organic compounds containing the groups  $-\text{NH}_2$ ,  $-\text{OH}$ ,  $-\text{COOH}$ ,  $=\text{NOH}$ , and  $=\text{NH}$  are abnormally high in non-polar solvents such as benzene, carbon tetrachloride, and naphthalene, and the apparent molecular weights increase as the concentration increases, while molecular weights of the same compounds in such solvents as acetic acid are often found to be normal. These facts are illustrated by figures 1 and 2 (8, 31). In these figures  $n$  represents

(apparent molecular weight)/(formula weight) and  $Q$  the concentration in formula weights per kilogram of solvent, unless otherwise indicated. Naphthalene and benzene are included for purposes of comparison. The freezing-point lowering constant for benzene has been taken to be 5.10 in all cases (32). The large abnormalities in non-polar solvents are interpreted as due to polymerization of the solute, while the normal molecular weights in water and acetic acid are interpreted in the usual way, as due

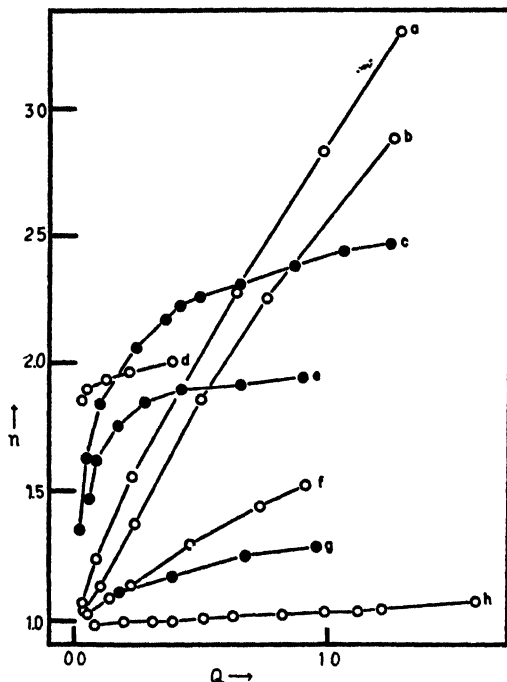


FIG. 1. Polymerization number plotted against concentration for typical polymerized solutes in benzene solution.  $Q$  in moles per kilogram of solution. a, formanilide; b, ethyl alcohol; c, acetoxime; d, benzoic acid; e, *d*-camphor oxime; f, benzhydrol; g, aniline; h, naphthalene.

to the reaction of the solute with solvent. The reaction of solute and solvent will not change the molal concentration of the solute, and hence will not affect a molecular weight determination by the freezing-point lowering method except in very concentrated solutions. This interpretation is a reasonable one from the hydrogen bond point of view because all the groups listed above could form hydrogen bonds with water or acetic acid. It is expected that such hydrogen bonds will be formed, owing to the large concentration of solvent, although polymerization need not disappear

completely in these solvents, and, in fact, does not always disappear, as we shall see later.

The polymerization discussed in the preceding paragraph depends upon the presence of a hydrogen atom attached to the proper sort of group. This is shown by the normal behavior of compounds containing the groups

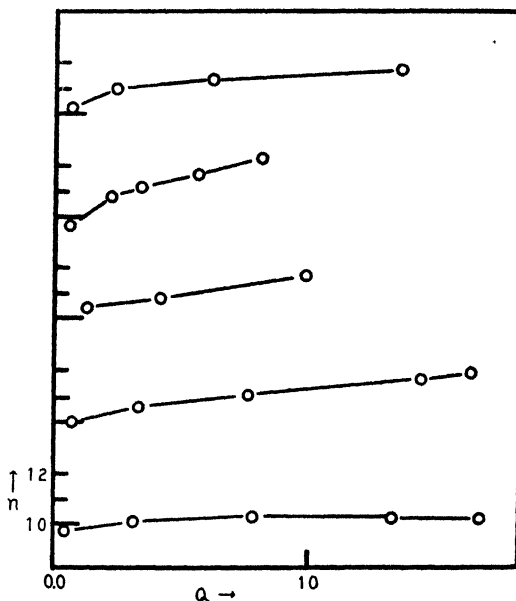
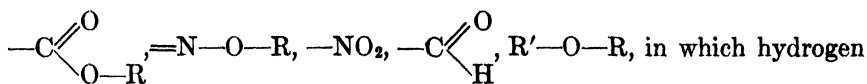


FIG. 2 The polymerization numbers of organic compounds in acetic acid solution.  $Q$  in moles per kilogram of solution. Reading from top to bottom: ethyl alcohol, benzhydrol, benzene, benzoic acid, acetoxime. The ordinate for the lowest curve is repeated for each of the upper curves.

has been replaced by another group, as illustrated by the data presented in figure 3 (8, 31). Although the apparent molecular weights of the compounds increase as the concentration increases, this increase is of the same order of magnitude as that found for naphthalene, and is therefore attributed to other causes than polymerization. The fact that the alcohols and phenol have normal molecular weights in water indicates that polymers of solute which are held together by molecules of water do not occur in these cases. Further, it seems that a large dipole moment is not sufficient to cause marked polymerization, since even such a strongly polar com-

pound as nitrobenzene does not show an abnormal molecular weight in benzene solution.

The data given in figures 1, 2, and 3 are not always from the most recent investigations, but instead are representative of the most extensive data in the literature.

One other fact concerning figure 1 should be noted, namely, that for acids and oximes the value of  $n$  appears to be approaching an upper limit,

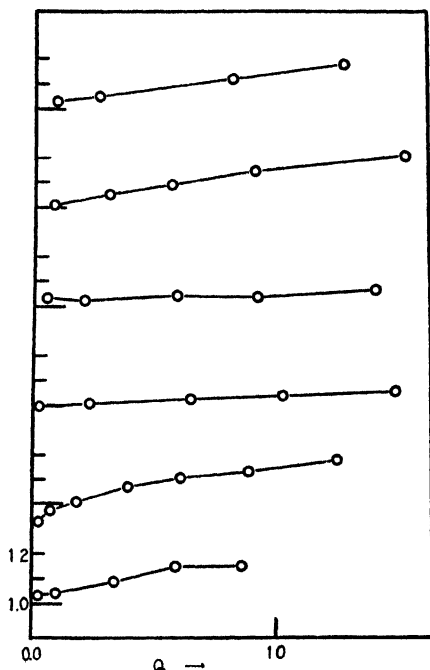


FIG. 3. Polymerization numbers of organic compounds which do not contain hydrogen attached to oxygen. The solvent is benzene.  $Q$  in moles per kilogram of solution. Reading from top to bottom: acetone, nitrobenzene, phenetole, ethyl benzoate, benzaldoxime ethyl ether, benzaldehyde. The ordinate for the lower curve is repeated for each of the upper curves.

while for alcohols, anilides, acid amides, and phenols the value of  $n$  increases indefinitely and almost linearly as the concentration increases. This indicates that polymers of low order are predominant in solutions of acids and oximes, while higher polymers occur in solutions of alcohols, anilides, etc. Of the two oximes shown, one appears to be approaching an upper limit of  $n = 2$ , while the second appears to be approaching an upper limit of  $n = 3$  or more. Both the dimer and trimer of these oximes would

probably be rings held together by hydrogen bonds of the N - - H—O type. That the trimers would occur in one case and not in the other might be due to a change in the  $\text{=N—O—H}$  bond angles in the two cases. These conclusions are borne out, for alcohols and acids, by distribution experiments which will be discussed shortly. The structures of the acid dimers are probably the same as that of formic acid. Neither molecular weight nor distribution data, except in very dilute solution, can be entirely accounted for by a dimer, so there may well be higher polymers in the solution.

The molecular weights of ethyl mercaptan, amyl mercaptan, and thiophenol have been investigated in benzene solution and found to be normal, indicating that the group  $\text{—S—H}$  does not form hydrogen bonds to any appreciable extent. A related conclusion, that  $\text{—OH}$  does not form hydrogen bonds to sulfur, is drawn from the fact that benzoic acid is found to be as largely polymerized in carbon disulfide solution as in benzene. A few hydrazones have been studied in naphthalene solution and found not to be appreciably polymerized (6).

#### V. EVIDENCE FROM MOLECULAR WEIGHT DETERMINATIONS FOR CHELATION IN AROMATIC COMPOUNDS

The investigations of the physical properties of the nitrophenols give evidence of another type of hydrogen-bond formation for which we shall use the name *chelation*.<sup>3</sup> Of their physical properties which have been investigated we shall consider in this section only the molecular weights.

A consideration of figure 4 (6) shows that the molecular weights of the *m*- and *p*-nitrophenols are abnormally high in naphthalene solution, while that of *o*-nitrophenol is normal. This difference in behavior of the ortho compounds is attributed to the formation of an internal hydrogen bond of the type shown in figure 5. The formation of an internal hydrogen bond would be expected to reduce the polymerization of *o*-nitrophenol, since the energy of this substance in the monomolecular form would be lowered by hydrogen-bond formation relative to non-chelated molecules, such as for *m*- and *p*-nitrophenol, whereas the ortho polymers would be about the same as the meta and para polymers, and hence the equilibrium between single molecules and polymers would lie farther towards single molecules for *o*-nitrophenol than for *m*- and *p*-nitrophenol. These experimental data indicate that a hydrogen atom already used to form a chelate ring cannot, at the same time, form a hydrogen bond to a neighboring molecule. The foregoing explanation was apparently first given by Sidgwick

<sup>3</sup> The term "chelation" is used by the English chemists to designate hydrogen bonds of all types. In this paper the term is used, for purposes of convenience, to designate only internal hydrogen-bond formation.



(36) and has been amply confirmed by the work of Wulf and collaborators from their study of absorption spectra.

The discussion of the nitrophenols shows that a study of molecular weights provides a means of detecting chelation in aromatic compounds. If the molecular weights of the meta and para compounds are abnormally

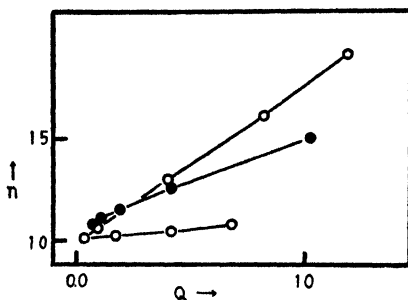


FIG. 4. Polymerization numbers of the nitrophenols in naphthalene solution. From top to bottom: *p*-, *m*-, and *o*-nitrophenol.

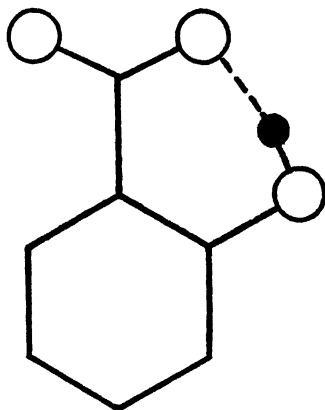


FIG. 5. Diagram of *o*-nitrophenol. The circles are oxygen atoms and the black dot is a hydrogen atom. The dimensions of the nitro group are those given by Brockway, Beach, and Pauling (11), while the other dimensions were obtained from a table of radii (30). The broken line represents a hydrogen bond.

high and increase with increasing concentration, while the molecular weight of the ortho compound is normal, it can be concluded immediately that the meta and para compounds form polymers through hydrogen-bond formation, and that the ortho compound is chelated. Figures 6a, 6b, and 6c (6) show the experimental data for the hydroxybenzaldehydes, the methyl esters of the hydroxybenzoic acids, and the azo compounds of phenol, re-

spectively, in naphthalene solution. From these figures it appears that the ortho compounds are all chelated and hence that the azo, aldehyde, and carboxylic ester groups are capable of forming hydrogen bonds with the hydroxyl hydrogen. These results are in agreement with those of Wulf and collaborators. It should be noted that the structures of the azo, aldehyde, and ester groups are such that a six-membered ring can be formed, similar to that for *o*-nitrophenol shown in figure 5.

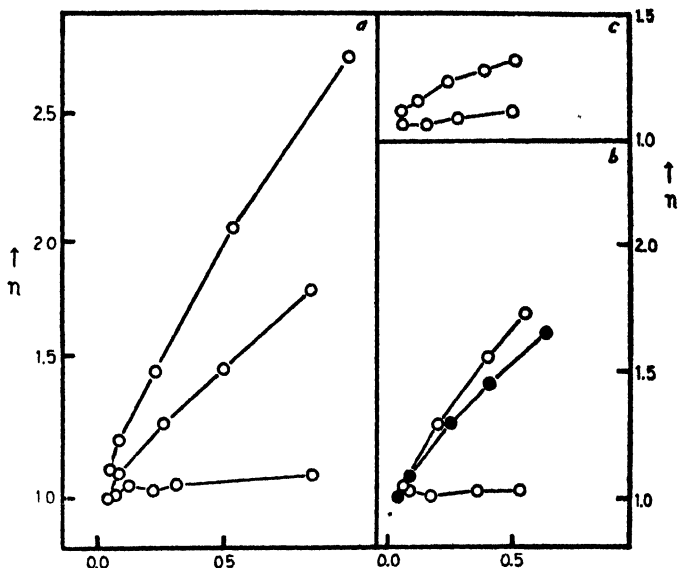


FIG. 6. (a) Polymerization numbers for the hydroxybenzaldehydes in naphthalene solution. Top to bottom: para, meta, ortho. (b) Polymerization numbers of methyl esters of the hydroxybenzoic acids in naphthalene solution. Top to bottom: para, meta, ortho. (c) Polymerization numbers of the azophenols in naphthalene solution. Top to bottom:  $\text{C}_6\text{H}_4\text{N}=\text{N}\text{C}_6\text{H}_4\text{OH}$ ,  $\text{C}_6\text{H}_4\text{N}=\text{N}\text{C}_6\text{H}_4\text{OH}$ . The HO  
H<sub>3</sub>C  
abscissae for a and b are the same.

All the preceding examples have been substituted phenols, but the phenomenon of chelation is not confined to these compounds. Compounds of the type



are apparently chelated when the group X is a nitro or aldehyde group, but the chelation is weak when X is a methoxyl group. These facts are

illustrated by the data presented in figure 7 (2) for compounds in naphthalene solution. The chelation is assumed to occur between the hydrogen of the amine group and the group X. The chelate rings contain six members in all cases shown, except the methoxy compound, which will be discussed later.

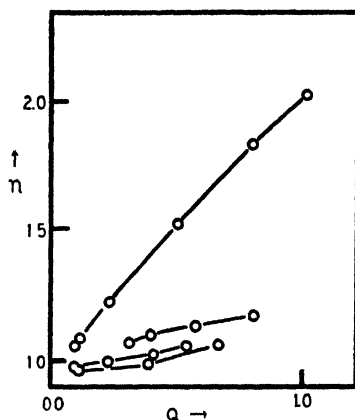


FIG. 7. Polymerization numbers of acetanilide and ortho-substituted acetanilides. Top to bottom:  $C_6H_5NHCOCH_3$ ,  $o-C_6H_4(OCH_3)NHCOCH_3$ ,  $o-C_6H_4(CHO)COCH_3$ ,  $o-C_6H_4(NO_2)NHCOCH_3$ .

TABLE 1  
Relative solubilities of *o*-, *m*-, and *p*-nitrophenols

Solvent. . . . .	H <sub>2</sub> O	H <sub>2</sub> O	C <sub>2</sub> H <sub>5</sub> OH	C <sub>4</sub> H <sub>9</sub> OH	CH <sub>3</sub> COCH <sub>3</sub>	Ether	C <sub>6</sub> H <sub>6</sub>	C <sub>6</sub> H <sub>6</sub>
Temperature. . . .	60°	20°	60°	60°	23°	17°	60°	20°C.
ortho/para . . . .	0 200	0 388	1 63	0 855	1 46	2.67	127.5	193 4
meta/para . . . .	0 739	1 84	1 03	0 560	1 17	1 03	1 04	2 76

## VI. THE GENERAL PHYSICAL PROPERTIES OF CHELATED COMPOUNDS

Several properties of chelated compounds are strikingly different from the properties of the non-chelated isomers in a way which can be interpreted from the hydrogen bond point of view.

It has been emphasized by Sidgwick that vapor pressures and solubilities of chelated compounds differ largely from those of the non-chelated isomers. For example, the vapor pressures at 100°C. of *o*-, *m*-, and *p*-nitrophenol are, respectively, 2.92 mm., 0.196 mm., and 0.083 mm. (37). To interpret these facts we consider the energy change attending a transfer of material from the liquid to the vapor phase. In liquid *m*- and *p*-nitrophenol hydrogen bonds exist between neighboring molecules, while in

liquid *o*-nitrophenol chelate bonds exist and hence the energies of all three isomers are approximately the same. In the vapor phase chelation will persist in *o*-nitrophenol, but the polymers of the *m*- and *p*-nitrophenols will tend to be dissociated, and therefore the energy absorbed upon vaporization of the meta and para compounds will be larger than for the ortho compound, thus leading to lower vapor pressures. In table 1 are shown the ratios of the solubilities of *o*- and *p*-nitrophenol, and of *m*- and *p*-nitrophenol in various solvents (38). Whereas the solubilities of the *m*- and *p*-nitrophenols are about the same in all solvents and the solubilities of the ortho, meta, and para compounds are roughly the same in the oxygenated solvents, the ortho compound is enormously more soluble in benzene than are the meta and para compounds. To find the reason for this behavior we consider the energy change occurring upon solution. The energies of the *o*-, *m*-, and *p*-nitrophenols as solids should be about the same,

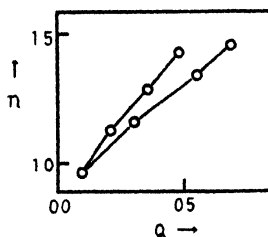


FIG. 8. Polymerization numbers of the nitrobenzylacetamides in naphthalene solution. Top to bottom:  $p\text{-C}_6\text{H}_4(\text{NO}_2)\text{CH}_2\text{NHCOCH}_3$ ,  $o\text{-C}_6\text{H}_4(\text{NO}_2)\text{CH}_2\text{NHCOCH}_3$ .

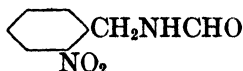
for the reason given above for liquids, and in an oxygenated solvent they should be about the same, since the meta and para compounds form bonds with the solvent while the ortho compound either remains chelated or forms bonds with the solvent. The energy changes are therefore about the same for all compounds in this case, and hence the solubilities should be about equal in oxygenated solvents. In benzene solution, however, the ortho compound remains chelated, while the meta and para compounds are dissociated; hence the energy absorbed by the meta and para compounds is larger and their solubility should be smaller.

Sidgwick and his coworkers (39) have investigated the phase rule diagrams of systems containing an organic component and water. It was found that when the organic component was chelated the critical solution temperature was much higher than for non-chelated isomers. The interpretation of this fact is apparently more complex than the interpretation of vapor pressure or solubility data.

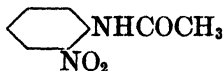
VII. EXAMPLES OF MOLECULAR WEIGHT STUDIES WHICH ILLUSTRATE THE STEREOCHEMICAL PROPERTIES OF HYDROGEN BONDS

The examples of section V have indicated some of the types of compounds in which six-membered chelate rings are found to occur. In this section examples showing the effect of varying the number of members in the chelate ring will be examined, together with others intended to illustrate the effect of varying bond angles and distances.

A consideration of figure 8 (2) shows that the compound



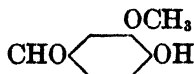
is not chelated to any large extent, while we have already seen that the compound



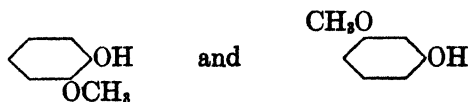
is strongly chelated. This difference in behavior is attributed to the fact that in the first case a seven-membered ring would have to be formed. We have already seen that the compound



is weakly chelated in naphthalene solution. In this compound only a five-membered ring can be formed. The compound



has been studied in naphthalene solution, and it was shown that although it is less polymerized than *p*-hydroxybenzaldehyde there is nevertheless some polymerization and hence the chelation is not complete. The results of molecular weight studies (4) on the two compounds



show that the ortho compound is chelated. These results indicate that the six-membered ring is somewhat more stable than the five-membered ring, and a seven-membered ring is much less stable than a five-membered one. The conclusions are expected to be dependent upon the bond angles

and internuclear distances in the ring. The general conclusions concerning the stability of the various rings are the same as those reached by Wulf and collaborators (20, 42) from their studies of absorption spectra. These investigators studied many more examples than are given here, and their conclusions are correspondingly more certain.

Figure 9 shows molecular weight data for *o*- and *m*-cyanophenol (6) and phenol in naphthalene solution. It is evident that the ortho compound is not chelated to any appreciable extent. It would be wrong, however, to conclude that the cyanide group is incapable of forming hydrogen bonds with the hydroxyl group, because from figure 12 we see that the introduction of the cyanide group into phenol enormously increases the polymerization. The reason for this apparently anomalous behavior is that the cyanide group is directed straight out from the benzene ring, and

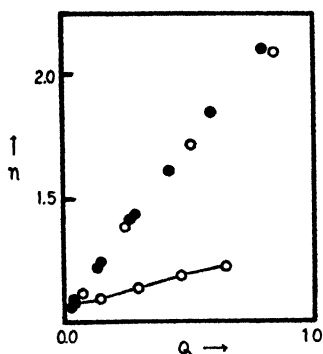


FIG. 9. Polymerization numbers of the cyanophenols in naphthalene solution. Upper curves: ●, *o*-cyanophenol; ○, *p*-cyanophenol. The lower curve is phenol.

hence the distance between oxygen and nitrogen becomes too great for a strong hydrogen bond to be formed.

In view of the preceding results it would seem reasonable to suppose that a dicarboxylic acid would tend to chelate, provided the hydrocarbon chain became long enough to permit the carboxyl groups to get close to one another. Measurements on the molecular weights of dicarboxylic acids in phenol by Robertson (34) have indicated that this is actually the case. The results of these experiments were not recorded directly by the investigator, who instead gave a number *A*, which is essentially the percentage change in polymerization number *n* for a lowering of 3.5°C. In table 2 are shown values of *A* for ethylmalonic, methylsuccinic, and sebacic acids; benzene is included for comparison purposes. Both ethylmalonic and methylsuccinic acids are polymerized, but sebacic acid is polymerized only slightly if at all. It can be shown by constructing a model that the hy-

drocarbon chain is long enough to permit chelation in sebacic acid, with eight carbon atoms in the chain between the carboxyl groups, but not in methylsuccinic or ethylmalonic acid.

From molecular weight measurements it is known that the polymerization numbers of benzoic, *o*-nitrobenzoic, and *m*-nitrobenzoic acids are approximately the same at a concentration of 0.5 molal in naphthalene solution (6), which indicates that there is no marked amount of chelation in *o*-nitrobenzoic acid. Since a seven-membered ring would have to be formed, it is not surprising that no marked chelation occurs. No molecular weight data exist for *o*-methoxybenzoic acid, but distribution experiments have been performed on this compound in both toluene and chloroform solutions (40). The attempt to determine the equilibrium constant for chloroform solution was unsuccessful, but in toluene solution the compound was found to be much less polymerized than benzoic acid. This indicates that the ortho compound is chelated, but the possibility of hydration renders the interpretation uncertain until more experimental data

TABLE 2  
*Association factors of dicarboxylic acids in phenol solution*

COMPOUND	A
Ethylmalonic acid . . . . .	31
Methylsuccinic acid . . . . .	47
Sebacic acid . . . . .	16
Benzene . . . . .	12

are available. It is to be noted that a six-membered ring could be formed in this case.

The relative vapor pressures of *o*-, *m*-, and *p*-hydroxybenzoic acids are 1320.0, 5.0, and 1, respectively, at 100°C. (35), indicating that the ortho compound is chelated (see section VI). On the other hand the relative vapor pressures of the *o*-, *m*-, and *p*-nitrobenzoic acids are 20.9, 7.3, and 1, respectively, at 100°C., indicating that the ortho compound is only weakly chelated if at all. These results confirm the relative stabilities of six- and seven-membered rings. Unfortunately it is not possible to say from these data whether the hydrogen involved in the chelate ring of *o*-hydroxybenzoic acid comes from the hydroxyl group or from the carboxyl group.

#### VIII. THE EFFECT OF CHANGE OF SOLVENT UPON THE MOLECULAR WEIGHTS OF DISSOLVED COMPOUNDS

The effect of change of solvent upon the molecular weights of dissolved materials was actively investigated in the early part of the twentieth century in connection with the hypothesis of Nernst that polymerization

is least in solvents of high dielectric constant. The general result of these investigations was to confirm this rule, and the results appear to be so well known that they will be omitted here unless they are intimately connected with the properties of the hydrogen bond.<sup>4</sup>

The earliest and perhaps the most complete systematic investigation of the effect of solvent change was that of Auwers (5). The solvents used were of the type  $\text{CH}_3\text{C}_6\text{H}_4\text{X}$ , where the X group was varied. The solutes used were substituted phenols and benzoic acids. The general result of this investigation was summarized by Auwers with the statement that the order of the groups in producing polymerization was  $-\text{CH}_3$ ,  $-\text{Cl}$ ,  $-\text{Br}$ ,  $-\text{I}$ ,  $-\text{NO}_2$ ,  $-\text{CO}_2\text{R}$ ,  $-\text{CN}$ ,  $-\text{CHO}$ ,  $-\text{NH}_2$ ,  $-\text{CO}_2\text{H}$ ,  $-\text{OH}$ . The groups furthest to the left were most effective in producing polymerization when in the solvent and least effective when in the solute. The experiments were rough, and in a few cases solid solutions seemed to be formed, but the order given has in general been confirmed by subsequent investigations. The position of the amino group in this series is a little surprising in view of the small polymerization of aniline in benzene solution (see figure 1). The result indicates that the amino group forms much stronger hydrogen bonds with other groups than with itself. This property of the amino group also makes itself felt in connection with other properties than polymerization (36).

The investigations of Meldrum and Turner (27) on the acid amides and anilides in the solvents benzene, chloroform, alcohol, acetone, ether, and water have shown that although polymerization proceeds about as expected in the first five solvents, the amides and anilides are much more widely polymerized in water than might be expected, and in fact those compounds which are least polymerized in benzene tend to be most polymerized in water. Of the solvents listed only alcohol and water have hydrogen atoms which can form hydrogen bonds, alcohol having one and water two. From the order of Auwers and the interpretation given to it, it seems reasonable to suppose that in case a solvent can donate two hydrogen atoms, one to each of two molecules of a solute, a polymer may be formed which is held together by a molecule of solvent. Water is the only such solvent among those listed and is at the same time that solvent in which most anomalies occur. For one compound, methylacetanilide, which contains no hydrogen which can form hydrogen bonds and hence for which no polymerization is expected, it is actually found that in benzene, chloroform, alcohol, acetone, and ether the molecular weight is normal, while in water the molecular weight is about three times the formula weight. This com-

<sup>4</sup> For an account of these results see Turner, *Molecular Association*, Longmans, Green and Co. (1915).



pound is appreciably volatile at the boiling point of water, but this fact was known to Meldrum and Turner and precautions were taken to reduce the error to a minimum, although the molecular weight was not actually corrected for the volatility of the solute. The opinion of the investigators was that the high molecular weight cannot be entirely accounted for by the volatility of the compound. If this result is correct it is difficult to see how this high molecular weight can be explained other than by assuming that two molecules of solute are held together by one of water. The experiments of Peddle and Turner (31) on the molecular weights of salicylic and benzoic acids in water solution deserve mention, because they provide an inconsistency which has not yet been explained. At the boiling point of water these acids have molecular weights approximately twice the formula weight, even after corrections have been applied for the volatility of the two acids. These experiments cannot as yet be said to contradict flatly the experiments on the distribution of benzoic and salicylic acids between benzene and water, because they were performed at a different temperature, but they come dangerously close to contradicting the distribution experiments. From molecular weight measurements in benzene such as those shown in figure 1 it is known that benzoic acid is probably not more than doubled in benzene at the freezing point, and hence the distribution experiments cannot be explained by assuming a doubled molecule in water and a quadrupled one in benzene. This contradictory evidence led Peddle and Turner to conclude that the polymerization of compounds in water solution was not a real effect but was due to some simplification in the structure of water caused by the addition of solute. This hypothesis seems unlikely, especially in view of the fact that Raoult's law has been verified for such a compound as mannite in water solution (17). The whole problem is now at a point at which more experimental investigation is called for.

The behavior of benzoic acid in a few of the more common solvents is shown by the data given in table 3 (9, 12). The number recorded is the mean polymerization number at a concentration of 0.5 mole per kilogram of solvent. The measurements were on the raising of the boiling point, except for that in nitrobenzene which was an experiment on the lowering of the freezing point. Benzoic acid is polymerized in all the non-polar solvents given and is not appreciably polymerized in any of the oxygenated solvents except nitrobenzene. Nitrobenzene behaves in the same fashion with other polymerizable compounds.

Experiments in pure solvents provide us with two extreme pieces of information at temperatures which are often widely different, one on the behavior in a pure non-polar solvent and the other on the behavior in a pure hydrogen-bond-forming solvent. It is desirable to have a complete

view of the isothermal changes in polymerization which occur when one goes continuously from one of these extreme cases to the other. Such a picture is obtained from a consideration of the experiments of Barger (7) on the molecular weights of compounds in mixed solvents. By means of an ingenious method Barger was able to measure the molecular weights of solutes in solvents which were mixtures of two components, of which one component was a non-polar material, such as benzene, and the other component a hydrogen-bond-forming material, such as an alcohol. A series of measurements upon a polymerizable solute was then made in a series of solvent mixtures of varying composition. A set of data typical of the results obtained, with a few exceptions, is shown graphically in figure 10. The concentration of solute is indicated in the legend and was kept constant in all measurements of a given series. As ordinate is plotted the

TABLE 3

*Polymerization numbers of benzoic acid (0.5 molal) in various solvents, with naphthalene for comparison*

SOLVENT	$\eta$ FOR BENZOIC ACID	$\eta$ FOR NAPHTHALENE
Acetone . . . . .	0.99	1.00
Acetic acid . . . . .	1.00	1.17
Ethyl ether . . . . .	1.04	0.98
Ethyl alcohol . . . . .	1.06	
Ethyl acetate . . . . .	1.09	1.04
Chloroform . . . . .	1.82	1.00
Benzene . . . . .	1.96	1.10
Carbon disulfide . . . . .	2.14	1.03
Phenol . . . . .	1.16	1.09
Nitrobenzene . . . . .	1.69	

mean polymerization number of solute and as abscissa the percentage composition of the solvent. The striking feature of the figure is that the introduction of a small amount of hydrogen-bond-forming solvent materially decreases the polymerization number. This can be interpreted most easily by assuming that the solvent combines with the solute and breaks up the polymer; this interpretation was given by Barger in 1905.

Figure 10 thus indicates that pyridine forms strong hydrogen bonds with formanilide. This is in complete agreement with the investigations of Innes (23), who showed that organic acids and related compounds have normal molecular weights in pyridine. Presumably these data can be analyzed by applying the law of mass action, but the solutions are so concentrated and the equilibria are so complex that this does not seem worth while.

The curve found by Barger for guaiacol in mixtures of methyl alcohol and chloroform shows a pronounced maximum at about 15 per cent alcohol. Guaiacol has already been shown to be a definitely chelated compound and its chelated character is borne out in this experiment, since in pure chloroform the polymerization number is small. Guaiacol was the only chelated compound investigated and the only one for which a maximum was observed, so it seems probable that the two are connected. An interpretation in terms of hydrogen bonds leads to the conclusion that the addition of methyl alcohol tends to break the chelate bond, but the experimental data are so incomplete that this conclusion is not justified at present. More investigation of this point would be desirable.

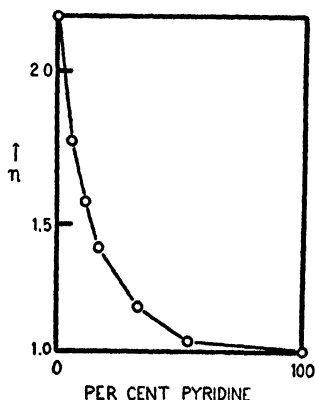


FIG. 10. Polymerization number of formanilide dissolved in mixtures of pyridine and toluene. The concentration of formanilide was 0.5 mole per liter of solution throughout. The percentage composition of solvent is plotted as abscissa.

#### IX. EXPERIMENTS UPON THE DISTRIBUTION OF HYDROGEN-BOND-FORMING COMPOUNDS BETWEEN TWO IMMISCIBLE SOLVENTS

In the distribution experiments which are considered here one phase is always water and the other an organic liquid. Interpretation of these experiments is always made by assuming that the molecules are single in the water phase, and polymerized, if at all, only in the organic phase. One of the most serious difficulties which attend the interpretation of distribution experiments is the possibility of hydration. Quantitative investigation of this factor has been made in recent years and a description of some of these results will be given first.

By studying the solubilities of certain organic acids in solutions of both dry benzene and benzene saturated with water Szyszkowski (41) has been able to correct the dissociation constants, obtained from distribution ex-

periments, for hydration. The increase in solubility of the acid gave directly the concentration of hydrated molecules. Since water is comparatively insoluble in benzene the solution will be dilute with respect to water, so it was assumed that the hydrate of most importance at these low concentrations is that containing one molecule of water. With these assumptions it is possible to compute the equilibrium constant for the dissociation of non-hydrated double molecules by a straightforward application of the law of mass action. In the course of these experiments Szyszkowski found that in order to account for the distribution ratio of *o*- and *m*-nitrobenzoic acids between water and benzene it is necessary to assume, in addition to a dimer, quadruple molecules in the benzene phase. The results are shown in table 4. The concentrations are in moles per kilogram. The letters shown in the table have the following meanings:  $K'$  is the equilibrium constant, uncorrected, of the reaction  $A_2 \rightleftharpoons 2A$ ,  $\Delta$  is the percentage change in solubility of the acid upon saturating benzene with water,  $K_2$  is the equilibrium constant of the reaction  $A_4 \rightleftharpoons 2A_2$ , and

TABLE 4

*Dissociation constants of aromatic acids from distribution ratios at 25°C.*

ACID	$K_2$	$K'$	$\Delta$	$K$
	<i>moles per kilogram</i>	<i>moles per kilogram</i>	<i>per cent</i>	<i>moles per kilogram</i>
Benzoic . . . . .		$2.63 \times 10^{-3}$	3.1	$4.74 \times 10^{-4}$
Salicylic . . . . .		$3.30 \times 10^{-3}$	31.2	$8.45 \times 10^{-3}$
<i>o</i> -Nitrobenzoic	$1.75 \times 10^{-2}$	$4.60 \times 10^{-2}$	60	$8.38 \times 10^{-3}$
<i>m</i> -Nitrobenzoic	0.70	$1.15 \times 10^{-2}$	26.7	$2.49 \times 10^{-4}$

$K$  is the corrected value of  $K'$ . The values of  $K$  differ considerably from those of  $K'$ . If we look at  $K'$  we conclude that *m*-nitrobenzoic acid is much less polymerized than salicylic acid, while if we look at  $K$  we arrive at the opposite, and correct, conclusion. This experiment indicates the need for caution in comparing the results of distribution experiments. An examination of the table shows that both salicylic and *o*-nitrobenzoic acids are less polymerized than benzoic acid, while *m*-nitrobenzoic acid is more polymerized, indicating that *o*-nitrobenzoic acid is weakly chelated.

Szyszkowski also investigated the question of whether these acids could form compounds with one another. This was done by measuring the solubility of mixtures of the two compounds. It was observed that the solubility of the mixture is greater than the sum of the solubilities of the separate acids. The excess is attributed to compound formation between the two acids and upon assuming that the combination is one to one the equilibrium constant,  $K_{12}$ , of the reaction  $AB \rightleftharpoons A + B$  is obtained. The constants  $K_{12}$  for various pairs are shown in table 5. The constants are

of the same order of magnitude as the dissociation constants of the dimers of the pure constituents, but otherwise seem to bear no particular relation to them.

This work illustrates the importance of investigating the question of hydration and indicates that distribution experiments which do not take this effect into account may give misleading results. In the present stage of experimental development distribution experiments are chiefly useful for detecting polymerization and for finding the relations between the equilibrium constants of successive polymers.

The general results of distribution experiments show that the organic acids can be considered as polymerized largely into doubled molecules, while

TABLE 5  
*Dissociation constants of mixed compounds of aromatic acids*

MIXTURE	$K_{12}$
Salicylic + <i>o</i> -nitrobenzoic acids.....	$6.30 \times 10^{-3}$
<i>m</i> -Nitrobenzoic + salicylic acids. . . . .	$2.19 \times 10^{-3}$
<i>m</i> -Nitrobenzoic + <i>o</i> -nitrobenzoic acids. . . . .	$8.94 \times 10^{-4}$

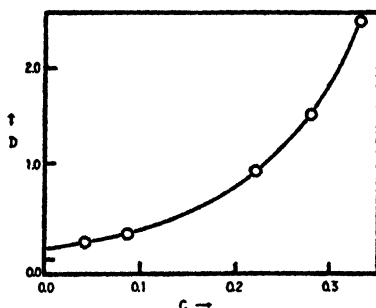


FIG. 11. Distribution of phenol between pentachloroethane and water

phenol polymerizes into high-order polymers. This fact is illustrated by figure 11, which shows the distribution ratio as a function of the concentration for phenol between water and pentachloroethane. If only a dimer were present the curve would be a straight line. In connection with the polymerization of phenol a recent investigation by Philbrick (33) of the distribution between water and several organic solvents shows a dimer of phenol to be present, except possibly in carbon tetrachloride solution. The investigations were made in very dilute solution, and it is shown that the distribution ratio is a linear function of the concentration in the water phase at low concentrations. This is just the behavior expected when a dimer is predominant. The equilibrium constants of the reaction  $2A \rightleftharpoons A_2$  for various solvents are shown in table 6. The order of solvents in

producing abnormalities is in agreement with that of Auwers. Philbrick also reported a sharp point of inflection in the distribution ratio curve at low concentrations, which has not previously been observed and which has not yet been completely accounted for. More extended investigation of this phenomenon is called for. The distribution ratio between carbon tetrachloride and water does not vary sufficiently to permit the calculation of an equilibrium constant.

The most extensive investigation of the distribution of organic acids between two solvents is that of Smith and White (40), who used the solvents toluene, chloroform, and benzene. The experiments were not corrected for hydration, and the equilibrium constants vary quite specifically with both solvents and substituents. This is illustrated by the fact that in toluene solution the dissociation constants of the dimers of *o*- and *p*-toluidic acids are  $22.3 \times 10^{-3}$  and  $1.74 \times 10^{-3}$ , respectively, while in

TABLE 6  
*The equilibrium constants for the dimer of phenol in various solvents*

SOLVENT	K
	<i>moles per liter</i>
$\text{C}_6\text{H}_5\text{CH}_3$ .....	0.843
$\text{C}_6\text{H}_5\text{Cl}$ .....	0.648
$\text{C}_6\text{H}_6$ .....	0.575
$\text{C}_6\text{H}_5\text{NO}_2$ ....	0.196

chloroform solution the constants are  $1.38 \times 10^{-3}$  and  $198.0 \times 10^{-3}$ , respectively, the order being completely changed. This fact and others like it discourage any attempt to interpret the results.

#### X. THEORY OF THE CALCULATION OF EQUILIBRIUM CONSTANTS FROM DATA ON THE LOWERING OF THE FREEZING POINT AND FROM DISTRIBUTION DATA

In the preceding sections data have been presented which indicate that the properties of solutions of organic acids can be satisfactorily accounted for by assuming equilibria between single and double molecules. There remains the problem of applying the law of mass action to solutions which contain higher polymers.

It is assumed that the solutions under discussion contain polymers constructed from some fundamental molecular unit designated by A, the polymer of order *l* being designated by  $A_l$ . The essential variables are as follows:

$Q$  = concentration in formula weights of A per kilogram of solvent,  
 $N$  = concentration in total moles of solute per kilogram of solvent,

$n$  = moles of solute per formula weight of A (evidently  $n = Q/N$ ),  
 $(A_i)$  = concentration of polymer  $A_i$  in moles per kilogram of solvent,  
 and

$K = (A_i)/(A)^i$  = equilibrium constant of the reaction  $lA \rightleftharpoons A_i$ .

The following three hypotheses are made: (i) Abnormalities (e.g., in freezing points) are due to the presence of polymers. (ii) The reactions involved are so rapid that equilibrium is completely established at the time of measurement. (iii) The polymers obey the law of mass action with all activity coefficients unity. These three hypotheses suffice for the proof of the following two mathematical theorems.

*Theorem A.* There exists one and only one set of constants  $K_i$  which leads to a relation between  $n$ ,  $Q$ , and  $N$  of the form

$$n = 1 + f(Q, N) \quad (1)$$

where  $f(Q, N)$  is a given continuous function with continuous derivatives of all orders,  $f(0, 0) = 0$ , and  $f(Q, N) \geq 0$ .

*Theorem B.* If  $f(Q, N)$  of equation 1 has the form

$$f(Q, N) = \alpha Q + \beta N \quad (2)$$

where  $\alpha$  and  $\beta$  are any constants independent of  $n$ ,  $Q$ , and  $N$ , the equilibrium constants are given by

$$K_l = \frac{1}{l!} \prod_{q=0}^{l-2} [\alpha l + \beta(l-q)], \quad q = 0, 1, 2, \dots, l-2; l = 1, 2, 3, \dots, \quad (3)$$

and in addition

$$N = (A)(1 + \beta N)^{\frac{\alpha+\beta}{\beta}} \quad (4)$$

In order that  $K_i$  be positive we must have  $\alpha + \beta > 0$ , and  $\alpha > 0$ .

The inverse of theorem A, namely, that to each set of constants there corresponds only one function  $f(Q, N)$ , is not true without further restrictions. This arises because  $N$  and  $Q$  are not independent. If we substitute the relation  $Q = nN$  in equation 1, we obtain  $n = 1 + f(nN, N)$ , and this equation can be solved for  $n$ , having, in general, several roots from which we must select that root which satisfies the condition that  $n = 1$  when  $N = 0$ . This will determine the root uniquely, and the resulting equation will have the form  $n = 1 + \phi(N)$ ,  $\phi(0) = 0$ . With the problem in this form only one function  $\phi(N)$  will correspond to a given set of constants  $K_i$  and vice versa. The same is true when we eliminate  $N$  from the equation instead of  $Q$ . These facts may be illustrated by using the special function equation 2. Making the substitution  $N = Q/n$  and solving for  $n$  we obtain

$$n = \{1 + \alpha Q \pm \sqrt{(1 + \alpha Q)^2 + 4\beta Q}\}/2$$

$n$  reduces to unity when  $Q = 0$  only provided we take the positive sign for the radical, hence

$$n = \{1 + \alpha Q + \sqrt{(1 + \alpha Q)^2 + 4\beta Q}\}/2$$

This matter is of some importance in actual applications of the theorems. It is to be noted that, subject to the restrictions outlined above, equation 1 determines one and only one curve in the  $n, Q$  plane, and hence, for example, any curve in figure 1 determines a unique set of  $K_i$ 's and vice versa.

The proofs of these theorems will be omitted, since they are given in detail in an article to be published elsewhere (24).

In applying these results to actual data the constants  $\alpha$  and  $\beta$  of equation 2 are to be determined by making use of measured values of  $n$ ,  $Q$ , and  $N$ ; specific methods of evaluating the constants are given in a subsequent section. Since equation 3 provides for an infinite number of constants, a discussion of the number of significant constants must be given, and this matter will be taken up in section XI in connection with a specific set of experimental data. Theorem A serves mainly to indicate the danger of an

TABLE 7  
Dependence of  $K_l$  on ratio of  $\alpha$  to  $\beta$  when  $\alpha + \beta = 2$

$\frac{\alpha}{\beta} =$	0 2	1 1	2 0	3 -1	4 -2	5 -3
$l = 2$	2	2	2	2	2	2
3	4	5	6	7	8	9
4	8	14	21 3	30	40	51 3
5	16	42	83 3	143	224	329 3

unrestrained discussion of experimental data from this point of view. Positive deviations from the laws of perfect solutions may well, and indeed do, arise from causes other than polymerization, and in these cases a treatment in terms of the above ideas would serve only to disguise the nature of the phenomena involved. It is necessary then to confine the treatment to cases for which the deviations are so large that they can be attributed only to polymerization.

If we let  $l = 2$  in equation 3 we obtain  $\alpha + \beta = K_2$ , which is the equilibrium constant of the reaction  $2A \rightleftharpoons A_2$ . This establishes the physical significance of the sum of  $\alpha$  and  $\beta$ . To study the physical significance of the ratio of  $\alpha$  and  $\beta$  we make the following calculation. We keep  $\alpha + \beta$  (that is,  $K_2$ ) constant but vary the ratio of  $\alpha$  to  $\beta$ ; the equilibrium constants  $K_l$ , with  $l > 2$ , are then found to increase steadily as  $\alpha$  increases and  $\beta$  decreases, the increase being larger for larger  $l$ . This is illustrated for the case  $\alpha + \beta = 2$  by table 7. It is seen that as  $\beta$  becomes more negative the higher equilibrium constants begin to predominate more and more strongly.



This is also reflected by the fact that if, using the relation  $n = Q/N$ , we plot  $n$  as a function of  $Q$  from equations 1 and 2 the curve is convex more and more sharply upward as the value of  $\beta$  becomes more negative.

It is interesting to examine the free energy change attending the addition of a single molecule to a polymer of order  $l$ , that is, the free energy change of the reaction  $A_l + A \rightleftharpoons A_{l+1}$ . The equilibrium constant of this reaction is

$$K'_l = \frac{K_{l+1}}{K_l}$$

In the limiting case  $\alpha = 0$  we obtain from equation 3

$$K'_l = \beta \quad (5)$$

This is just the relation expected when both the partial molal entropy and the partial molal heat content of a polymer are linear functions of the number of molecules in the polymer. This result is therefore a very reasonable one, particularly in view of the fact that the entropies and heat contents of the liquid normal paraffin hydrocarbons have been found by experiment to be nearly linear functions of the number of carbon atoms and, in fact, the thermodynamic constants of many organic compounds are known to be additive.

In the limiting case  $\beta = 0$  we obtain

$$K'_l = \alpha \left( \frac{l+1}{l} \right)^{l-1} \quad (6)$$

This is seen to vary with  $l$ , in contrast to equation 5, but the factor  $\left( \frac{l+1}{l} \right)^{l-1}$  varies only slowly, going from unity at  $l = 1$  to  $2.718 \dots$  at  $l = \infty$ . The behavior of  $K'_l$  is therefore not greatly different in the two cases  $\alpha = 0$  and  $\beta = 0$ . In both cases equation 3 gives results which are intuitively attractive. It should be noted, however, that the appearance of the curve for  $n$  plotted against  $Q$  is so greatly different in the two cases that we can easily distinguish between them.

The application of theorem B to data on freezing-point lowering is relatively simple, since both  $n$  and  $Q$  are directly determined. The application of this theorem to the calculation of equilibrium constants from distribution ratios is, however, much more laborious. A simple theorem can be proved which facilitates somewhat the numerical calculation of  $\alpha$  and  $\beta$ . It is assumed as usual that the material distributed is polymerized

in the organic layer but not in the water layer. The following variables are useful:

- $Q$  = concentration in organic layer in formula weights of A per unit volume or mass as the case may be,  
 $C$  = concentration in the water layer,  
 $x$  = concentration of single molecules in the organic layer,  
 $k = C/x$  = distribution constant,  
 $D = Q/C$  = distribution ratio, and  
 $N$  = concentration in organic layer in moles per unit of solution.

*Theorem C.* The molal concentration of solute in the organic layer is given by

$$N = \int_0^C D \, dC \quad (7)$$

The proof of this theorem can be made by methods entirely analogous to those used for theorems A and B. To obtain  $N$  it is necessary to plot  $D$  as a function of  $C$  and integrate graphically. Having determined  $N$ , theorem B can be applied as soon as  $\alpha$  and  $\beta$  are determined.

In the limiting case when  $\alpha = 0$ , the calculation of  $\beta$  from distribution experiments is especially simple. In this case by making use of equations 1, 2, and 4, and of the fact that  $C = kx$ , we easily obtain

$$\sqrt{\frac{1}{D}} = k^{\frac{1}{2}} - k^{-\frac{1}{2}}\beta C \quad (8)$$

In this equation  $k$  and  $\beta$  are constants and hence a plot of  $\sqrt{1/D}$  against  $C$  will give a straight line when the equation is applicable. From the slope and intercept of the line both  $\beta$  and  $k$  are obtainable.

#### XI. THE RELATIONS BETWEEN THE EQUILIBRIUM CONSTANTS OF SUCCESSIVE POLYMERS

The possibility of obtaining a general relation between the equilibrium constants of successive polymers directly from the experimental data, as discussed in the foregoing section, is a particularly interesting one. To obtain a reliable relation, very accurate data must be available. A definite conclusion is warranted in only a very few cases, which will be discussed in the following pages of this section, and the general applicability of equation 2 to distribution and freezing-point data will be examined.

In figure 12 data are shown for *p*-nitrophenol in naphthalene solution (2, 5, 1). At low concentrations the data are inconsistent, but it seems

that to a good approximation  $n$  is a linear function of  $Q$  and hence the relation 3 with  $\beta = 0$  is valid, giving for the equilibrium constants

$$K_l = \frac{(\alpha l)^{l-1}}{l!}$$

The question of the error involved in this relation is one to which no definite answer can be given; it can only be asserted that relation 3 with  $\beta = 0$  must exist in order to account in terms of polymerization for a linear relation between  $n$  and  $Q$ . We can, however, obtain a rough upper limit to the number of polymers to which equation 3 can be applied (24). This number is obtained by considering how many equilibrium constants can be omitted without introducing an error larger than the experimental error in  $n$ . The highest measured value of  $Q$  is 2.89, and  $n$  deviates from the

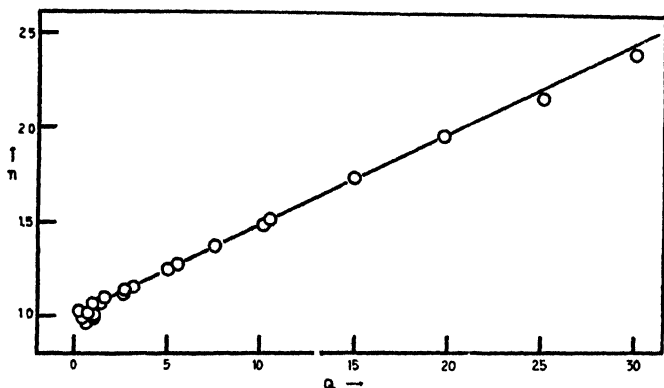


FIG. 12. Polymerization number of *p*-nitrophenol in naphthalene solution.  $Q$  in grams per hundred grams of solvent.

straight line by 0.06 unit. If we adopt 0.06 as experimental error it turns out that nine equilibrium constants are needed to account for the results to within the experimental error. It is to be emphasized that this does not mean that the first nine equilibrium constants are given by equation 3, but it does imply that we are not justified in applying equation 3 beyond  $l = 9$ .

Figure 13 shows data for *p*-nitrophenol in *p*-dibromobenzene (3), and here again the relation appears to be accurately linear. The line does not approach  $n = 1.00$ , but approaches  $n = 1.03$ . This fact is attributed here to a small error in the molal freezing-point lowering constant and is therefore ignored.

Brown and Bury (12) have determined the molecular weights of benzyl and isoamyl alcohols in nitrobenzene, using a technique which had pre-

viously been subjected to a very careful investigation. By performing the experiments both in the presence of a salt hydrate and in the presence of water the water content of the nitrobenzene could be controlled accu-

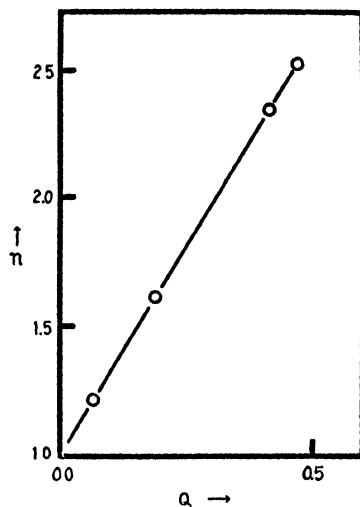


FIG. 13 Polymerization number of *p*-nitrophenol in *p*-dibromobenzene solution

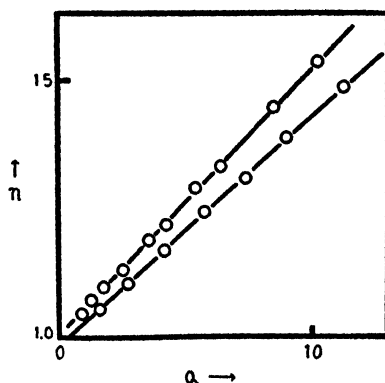


FIG. 14. Polymerization number of benzyl alcohol in nitrobenzene solution. Upper curve, dry nitrobenzene; lower curve, fully saturated nitrobenzene.  $Q$  is in grams per hundred grams of solvent.

ately. Their results for benzyl alcohol in dry nitrobenzene and in fully saturated nitrobenzene are shown in figure 14. The lines are straight, although they miss the origin by about 1 per cent, which is attributed to an error in the freezing-point constant. The curves for isoamyl alcohol

in nitrobenzene show a distinct curvature, so the general form of equation 2 must be used. If the substitution  $N = Q/n$  be made in equation 2 it can be readily verified that

$$\frac{n(n-1)}{Q} = \beta + \alpha n$$

hence by plotting  $n(n-1)/Q$  against  $n$  a straight line will be obtained when the equation is applicable. When  $n$  is close to unity the term  $(n-1)$  may be largely in error, so the low concentration points are expected to exhibit considerable irregularities, and, in fact, this method of plotting

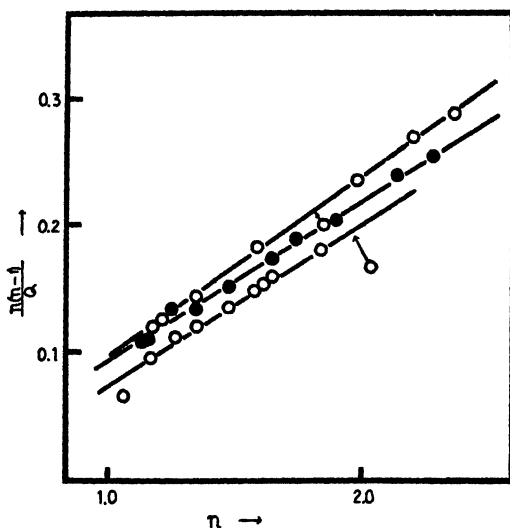


FIG. 15.  $n(n-1)/Q$  plotted against  $n$  for isoamyl alcohol in nitrobenzene.  $Q$  is in grams per hundred grams of solvent. Top to bottom: fully saturated nitrobenzene, partially saturated nitrobenzene, dry nitrobenzene.

will in general considerably magnify any irregularities in the data. In figure 15 the data for isoamyl alcohol in dry, partially wet, and completely saturated nitrobenzene are shown. The points are somewhat irregular, but on the whole the relation seems to be a linear one, and we conclude accordingly that equation 2 represents the data satisfactorily.

Experiments upon the distribution of phenol between water and organic solvents also indicate that equation 2 is applicable. In table 8 are shown the calculated and observed values of the distribution ratios of phenol between water and pentachloroethane. It will be observed that the agreement is within 1 per cent (see also figure 11). Figure 16 shows  $\sqrt{1/D}$

against  $C$  for phenol in toluene, and the line is approximately straight. Data for phenol between water and  $m$ -xylene have been examined and equation 2 is found to be roughly applicable, although the number of experimental points is too small to permit an accurate graphical integration. Data are available for phenol between benzene and water; however, the

TABLE 8  
*Distribution ratio of phenol between water and pentachloroethane*  
 $k = 1.085; \alpha = 0.83; \beta = 0$

$Q$ moles per liter	$D_{\text{obsd.}}$	$D_{\text{calcd.}}$
0.0495	1.18	1.17
0.110	1.27	1.28
0.226	1.51	1.51
0.432	1.94	1.92
0.708	2.53	2.56
1.170	3.51	3.50

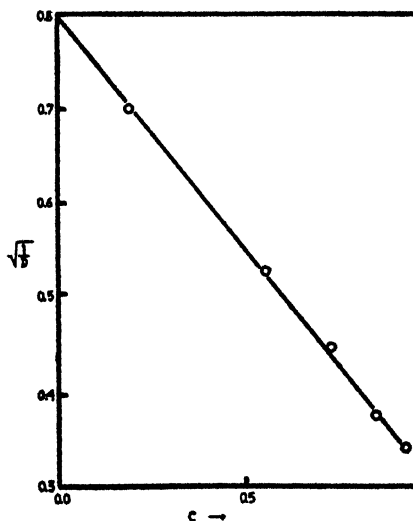


FIG. 16. Distribution of phenol between water and toluene.  $C$  is in moles per liter of solution.

highest concentration of phenol in benzene is 6 moles per liter of solution, and at such a concentration considerable deviations from the law of mass action are expected, so  $\beta$  was arbitrarily placed equal to zero in order to facilitate the calculation. The relation obtained in this way fits the data only to within about 5 per cent, but despite this fact the equilibrium

constants are in surprisingly good agreement with those of Philbrick (see table 6).

The constants  $\alpha$  and  $\beta$  from both the molecular weight and distribution data are collected in table 9.<sup>5</sup> In these cases, with the possible exception of phenol in benzene, it has been definitely shown that the equilibrium constants are given by equation 3, although the accuracy becomes less as  $l$  becomes larger. In toluene solution the constants do not agree with those of Philbrick, as is expected, since he reports a discontinuity in the distribution ratio curve at low concentrations in this solvent.

Equation 2 has been found to be capable of accounting for a large part of the existing data on anilides, amides, and substituted phenols in the

TABLE 9

*Equilibrium constants from distribution and molecular weight data*

COMPOUND	SOLVENT	$\alpha$	$\beta$	$K_2 = \alpha + \beta$
A. From molecular weight experiments (freezing point)				
Benzyl alcohol . . .	C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub> (fully saturated)	0 45		0 45
Benzyl alcohol . . .	C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub> (dry)	0 55		0 55
Isoamyl alcohol . .	C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub> (fully saturated)	1 29	-0 51	0 78
Isoamyl alcohol . .	C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub> (partially saturated)	1 11	-0 30	0 81
Isoamyl alcohol . .	C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub> (dry)	1 28	-0 71	0 57
<i>p</i> -Nitrophenol . . .	Naphthalene	0 67		0 67
<i>p</i> -Nitrophenol . . .	<i>p</i> -Dibromobenzene	3 18		3 18
B. From distribution experiments at 25°C.				
Phenol . . . . .	Pentachloroethane	0 83		0 83
Phenol . . . . .	Benzene		+0 58	0 58
Phenol . . . . .	Toluene		+0 67	0 67
Phenol . . . . .	<i>m</i> -Xylene	0 13	+0 16	0 29

cases for which the data are regular and approach the origin properly. This is illustrated by figures 17 and 18, which show data for formanilide in several solvents and *p*-hydroxybenzaldehyde in naphthalene solution. The data are from freezing-point measurements in all cases (6, 3). The lines are straight to within the limits of experimental error, and it is concluded that equation 2 fits the data satisfactorily.

Since equation 2 seems to be sufficiently adjustable, it has been used to calculate the equilibrium constants from the experimental data in all cases except for the aliphatic alcohols, which will be discussed later.

<sup>5</sup> All distribution data are from *International Critical Tables*, except that for pentachloroethane.

## XII. CALCULATION OF EQUILIBRIUM CONSTANTS FROM MOLECULAR WEIGHT DATA FOR THE SUBSTITUTED PHENOLS, AND THE RELATIVE STRENGTHS OF HYDROGEN BONDS

In the discussion which follows, an attempt has been made to avoid the inclusion of data which are more than usually irregular or for which the number of experimental points is unusually small. Since the results of these calculations are of interest chiefly for comparative purposes, the applications are confined to a few well-known solvents in which a variety of compounds have been investigated.

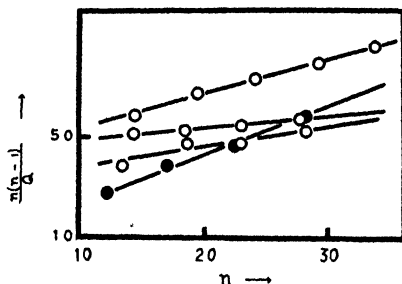


FIG. 17.  $n(n-1)/Q$  against  $n$  for formanilide in various solvents. Top to bottom: *p*-xylene, *p*-dichlorobenzene, *p*-dibromobenzene, benzene.

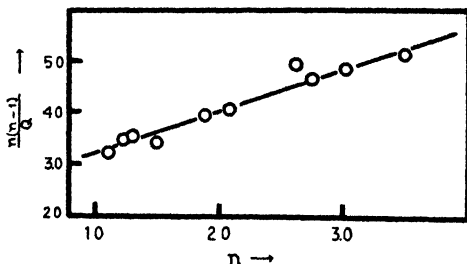













FIG. 18.  $n(n-1)/Q$  against  $n$  for *p*-hydroxybenzaldehyde in naphthalene solution

The material presented in section VI made evident the fact that introduction of a nitro group into the meta- or para-position of phenol considerably increases the polymerization number of the compound. This fact has a simple interpretation in terms of isomerism, which will be tested in this section. A para-substituted phenol of the type  $\text{XC}_6\text{H}_4\text{OH}$  can polymerize in two ways to form a dimer, either as  $\text{XC}_6\text{H}_4\text{OH} \cdots \text{HOC}_6\text{H}_4\text{X}$  or as  $\text{XC}_6\text{H}_4\text{OH} \cdots \text{XC}_6\text{H}_4\text{OH}$ , if the group X is capable of forming hydrogen bonds with the hydroxyl group. Let the equilibrium constants be  $K_2^{(1)}$  and  $K_2^{(2)}$ , respectively. By means of a simple application of the



law of mass action it is found that the equilibrium constant obtained from the data is  $K_2 = K_2^{(1)} + K_2^{(2)}$ . If a reasonable estimate of the constant  $K_2^{(1)}$  can be made,  $K_2^{(2)}$  can be calculated. We notice that the first isomer is held together by a bond between the two hydroxyl groups, and hence it seems reasonable to evaluate the constant  $K_2^{(1)}$  by considering a compound containing a group X which does not form hydrogen bonds.

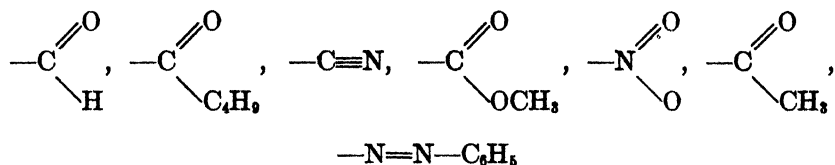
TABLE 10  
*Equilibrium constants for phenol, o-cresol, and para-substituted phenols in naphthalene solution*

COMPOUND	$\alpha$ (moles per kg. of solvent) <sup>-1</sup>	$\beta$ (moles per kg. of solvent) <sup>-1</sup>	$K_2 = \alpha + \beta$	$K_2^{(2)}$
 OH	0.30*			
CH <sub>3</sub>  OH	0.20	0.18	0.38	
CH <sub>3</sub>  OH	0.20*			
CH <sub>3</sub> OOC  OH	1.33	0.00	1.33	0.95
CN  OH	1.00	0.63	1.63	1.25
CHO  OH	0.82	2.45	3.27	2.89
 N=N  OH	0.94	-0.59	0.35	-0.03
O <sub>2</sub> N  OH	0.67	0.00	0.67	0.29
CH <sub>3</sub> CO  OH	1.06	-0.46	0.60	0.22
C <sub>6</sub> H <sub>5</sub> CO  OH	0.86	1.65	2.51(?)	2.13

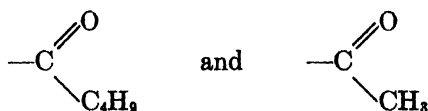
\*  $\beta$  was arbitrarily put equal to zero in these cases.

As such a compound *p*-cresol may be selected. The same considerations hold, of course, for meta-substituted phenols as well.  $K_2^{(2)}$  is clearly the equilibrium constant of a reaction which involves the formation of a bond of the type —X---H—O— and hence is a convenient measure of the bond strength. The equilibrium constants for a number of para-substituted phenols calculated from freezing-point lowering measurements (6, 3)

are shown in table 10. Equation 2 was used to fit the data in all cases, and the values of  $K_2$  are probably not reliable to more than  $\pm 0.05$  unit. If the hypothesis that the constant  $K_2$  for *p*-cresol is equal to  $K_2^{(1)}$  is satisfied, then  $K_2^{(2)}$  should never be negative. Actually, it does become negative in one case, for *p*-hydroxyazophenol, but the negative value is smaller than the experimental error and so is not significant. From a consideration of the constants  $K_2$  for phenol and *o*-cresol it seems likely that the estimate of  $K_2^{(1)}$  from the data for *p*-cresol gives too high a value. The strengths of the bonds between hydroxyl groups and other groups are in the order

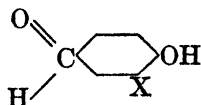


### The relative positions of the groups



are surprising, and indicate that other effects than isomerism contribute to the increase in polymerization number. Otherwise the order is in agreement with that of Auwers.

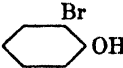
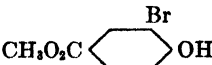
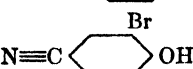
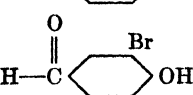
Table 11 shows a set of constants calculated from freezing-point lowering measurements (6) for para-substituted phenols which have a bromine in the position ortho to the hydroxyl group, while table 12 shows constants for a series of compounds (6) of the type



From table 12 we see that the constants decrease steadily in the order H, CH<sub>3</sub>, Br, OCH<sub>3</sub>, to such a low value as to indicate that the last compound is definitely chelated. This decrease in  $K_2$  upon introducing a substituent may be due to changes in bond energy and entropy, or it may be due to conversion of a constant fraction  $\alpha$  of molecules into such a form that they can not form hydrogen bonds to their neighbors. The equilibrium constants cannot decide the relative importance of these factors, of course, but it is of interest to make a calculation based on the last hypothesis and on the assumption that the introduction of bromine has no other

TABLE 11

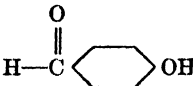
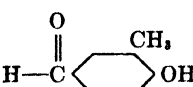
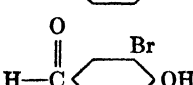
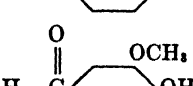
*Ortho-brominated substituted phenols in naphthalene solution\**

COMPOUND	$K_2 = \alpha + \beta$	$K_1^{(n)}$
	0 07	
	0 13(?)	0 06
	0 33	0 25
	0 70	0 63

\* The molecular weight data for these compounds consist of only a few points covering a small range of concentrations, and hence higher constants than  $K_2$  cannot be significant. The values of  $\alpha$  and  $\beta$  are accordingly omitted. The method of least squares was used to fit the data.

TABLE 12

*Equilibrium constants for the ortho-substituted p-hydroxybenzaldehydes in naphthalene solution*

COMPOUND	$\alpha$ (moles per kilogram of solvent) <sup>-1</sup>	$\beta$ (moles per kilogram of solvent) <sup>-1</sup>	$K_2 = \alpha + \beta$
	0 82	2 45	3 27
	1 55	0	1 55
	0.14	0 57	0 71
	0.32	0	0.32

effect. Using the equilibrium constants of tables 10 and 11 we obtain the values of  $a$  shown in table 13. If the hypothesis is valid these numbers should be equal, and we see that they are closely similar. Owing to sys-

TABLE 13

*Values of  $\alpha$  for ortho-brominated compounds in naphthalene*

OBTAINED FROM	$\alpha$
$\text{H}-\overset{\text{O}}{\parallel}{\text{C}}-\text{C}_6\text{H}_4\text{Br}$ and $\text{H}-\overset{\text{O}}{\parallel}{\text{C}}-\text{C}_6\text{H}_4\text{OH}$	0.52
$\text{N}\equiv\text{C}-\text{C}_6\text{H}_4\text{Br}$ and $\text{N}\equiv\text{C}-\text{C}_6\text{H}_4\text{OH}$	0.56
$\text{CH}_3\text{OC}(=\text{O})-\text{C}_6\text{H}_4\text{Br}$ and $\text{CH}_3\text{OC}(=\text{O})-\text{C}_6\text{H}_4\text{OH}$	0.69
$\text{C}_6\text{H}_4\text{Br}$ and $\text{CH}_3-\text{C}_6\text{H}_4\text{OH}$	0.56

TABLE 14

*Equilibrium constants for meta-substituted phenols and catechol in naphthalene solution*

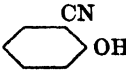
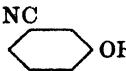

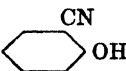
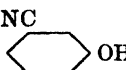

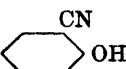

COMPOUND	$\alpha$ (moles per kilogram of solvent) <sup>-1</sup>	$\beta$ (moles per kilogram of solvent)	$K_2 = \alpha + \beta$
$\text{CH}_3\text{O}-\text{C}_6\text{H}_4\text{OH}$	0.44		0.44
$\text{O}_2\text{N}-\text{C}_6\text{H}_4\text{OH}$	1.12	0.71	1.83
$\text{CH}_3\text{OOC}-\text{C}_6\text{H}_4\text{OH}$	0.67	0.59	1.26
$\text{OHC}-\text{C}_6\text{H}_4\text{OH}$	0.41	0.92	1.33
$\text{OH}-\text{C}_6\text{H}_4\text{OH}$	1.04		1.04
$\text{OH}-\text{C}_6\text{H}_3(\text{OH})$	0.63	0.09	0.72

tematic deviations from the law of perfect solutions the constants in table 11 are no doubt too large, and hence the values of  $\alpha$  in table 13 are too small. It should be pointed out that the numbers in table 13 seem much too small to account for even a weak chelate bond.

In table 14 constants are shown for some meta-substituted phenols (6). In this case the order of the groups is changed, indicating again that effects other than isomerism are important in these polymerizations.

Table 15 shows equilibrium constants for the *o*-, *m*-, and *p*-cyanophenols in three solvents. The constants are calculated from freezing-point lower-

TABLE 15  
*Equilibrium constants for the cyanophenols in various solvents*

COMPOUNDS	$\alpha$	$\beta$	$K_2 = \alpha + \beta$
(a) Cyanophenols in <i>p</i> -dibromobenzene			
	(moles per kilogram of solvent) <sup>-1</sup> 2.1	(moles per kilogram of solvent) <sup>-1</sup> -0.6	1.5
	1.7	0.9	2.6
	1.9	3.2	5.1
(b) Cyanophenols in <i>p</i> -dichlorobenzene			
	5.0	-1.0	4.0
	3.3	2.5	5.8
	4.4	9.4	13.8(?)
(c) Cyanophenols in naphthalene			
	1.3	0.2	1.5
	1.0	0.6	1.6

















ing experiments (6, 3, 5). The compounds are all more polymerized in *p*-dichlorobenzene than in *p*-dibromobenzene. This difference can be attributed to the difference in the melting points of the two solvents, and, in fact, the magnitude of the difference is just that predicted by the van't Hoff equation by assuming a reasonable value of  $\Delta H$ . The small values of the constants in naphthalene solution can not be attributed to a tempera-

ture effect, and hence must be due to some specific interaction of the solute and solvent. Since addition compounds of naphthalene with various aromatic compounds are known, the effect may be due to an actual combination of solute and solvent. The steady decrease in the dimer constant from the ortho to the para compound indicates a steric effect which becomes less important as the cyanide radical is moved away from the hydroxyl group.

Considering the quality of the available data, the interpretations in this section seem moderately satisfactory. The indications are, however, that the interpretation of such data as these awaits further advances in experimental investigations of the structure of polymers.

TABLE 16

*Equilibrium constants of anilides, acid amides, and azophenols in naphthalene solution*

COMPOUND	$\alpha$	COMPOUND	$\alpha$
 NH <sub>2</sub>	0.14	 N=N  OH	0.66
 NHCHO	0.77	 N=N  OH	0.28
 NHCOCH <sub>3</sub>	0.96	 N=N  OH	0.90
 NHCOOCH <sub>3</sub> OCH <sub>3</sub>	0.23	 N=N  OH	0.32
CH <sub>3</sub> O  NHCOOCH <sub>3</sub>	1.13	 CONH <sub>2</sub>	1.44
 N=N  OH	0.50		

### XIII. EQUILIBRIUM CONSTANTS FOR COMPOUNDS OTHER THAN SUBSTITUTED PHENOLS

#### A. Azophenols, anilides, and acid amides

The existing data on the azophenols, anilides, and acid amides are both less extensive and less accurate than on the substituted phenols, so a treatment analogous to that of section XIII can not be carried out for these compounds. Furthermore, the data offer nothing essentially new, so only a few examples will be considered in order to show the order of magnitude of the equilibrium constants. In table 16 are shown the equilibrium constants calculated from freezing-point experiments (2, 6) for a few of these compounds in naphthalene solution. The data were fitted reason-

ably well by a straight line, so  $\beta$  was arbitrarily placed equal to zero. The only surprising feature is the great difference between the methoxy compounds of *p*-hydroxyazobenzene, and no reason is known for this behavior. Table 17 shows data for three normal acid amides in benzene solution. The constants were calculated from boiling-point raising experiments (27). The data for these three compounds are fitted best by assuming that  $\alpha = 0$ , and the amides are the only compounds which are fitted at all well with  $\alpha = 0$ .

Data for formanilide exist at both the freezing point and boiling point in benzene solution (5, 27), so it should be possible to calculate  $\Delta H$  for the dimer formation. The equilibrium constant at the freezing point is  $K_2 = 2.4$ , and at the boiling point  $K_2 = 0.8$ , hence  $\Delta H = -2900$  cal. per mole. A structure of the dimer of formanilide can be written which involves two  $-\text{N}-\text{H}-\text{O}-$  bonds, but this structure seems somewhat unlikely in view of the small value for  $\Delta H$ . At the boiling point only three experimental points were available, so the value is highly uncertain.

TABLE 17  
*Acid amides in benzene solution (boiling-point measurements)*

COMPOUND	$\beta$ (moles per liter of solvent) <sup>-1</sup>
$\text{C}_2\text{H}_5\text{CONH}_2$ .. .. .	3.9
<i>n</i> - $\text{C}_4\text{H}_9\text{CONH}_2$ .....	3.6
<i>n</i> - $\text{C}_6\text{H}_{13}\text{CONH}_2$ .....	2.7

### *B. The aliphatic alcohols*

The data for the aliphatic alcohols, which seemed at first to be the most easily interpreted, have proved to be rather confusing. As has been pointed out before, the curve for ethyl alcohol in benzene shown in figure 1 exhibits a tendency toward a point of inflection. This tendency is apparently a real one, since the molecular weight of ethyl alcohol in dilute solutions of benzene has been shown by the work of Peterson and Rodebush (32) to be constant and normal at low concentrations. The relation between the equilibrium constants is therefore more complicated than any that has yet been investigated. These data are even more remarkable, in view of the fact that the molecular weight of methyl alcohol is found by Peterson and Rodebush to increase rapidly even at very low concentration. These two examples illustrate the vital need for low concentration data in all cases. Because of the difference in behavior of methyl and ethyl alcohols even in very dilute solution, the data for these compounds have not been treated quantitatively. Data for a few higher alcohols have been

analyzed under the specific hypothesis that the curve approaches the origin with a slope which is different from zero. Under this hypothesis it is found that the data for several higher alcohols can be represented by a function of the form  $n = 1 + \alpha + RN^P$ , where  $\alpha$  and  $R$  are constants and  $P$  is an integer; these constants must be determined from experimental data. Application of the methods of section X shows that the equilibrium constants are

$$K_l = \frac{(\lambda\alpha)^{l-1}}{l!} \quad \text{if } l - 1 < P$$

but

$$K_l = \frac{(\lambda\alpha)^{l-1}}{l!} + \frac{R}{P} \quad \text{when } l = P + 1$$

TABLE 18

*Equilibrium constants of normal aliphatic alcohols in benzene solution*

COMPOUND	$\alpha$	$R$	$P$
	(moles per kilogram of solvent) <sup>-1</sup>		
<i>n</i> -Propyl alcohol . . . . .	1 56	-12	5 1
<i>n</i> -Butyl alcohol . . . . .	1 63	-6	4 0
<i>n</i> -Heptyl alcohol . . . . .	1 80	-10	4 0
<i>n</i> -Octyl alcohol . . . . .	1 61	-12	4 1

The first  $P$  equilibrium constants are unaffected by the term  $RN^P$ . In table 18 (10) are shown values of  $\alpha$ ,  $R$ , and  $P$  for four alcohols. These values must be considered tentative until the molecular weights at low concentration have been investigated. In the cases shown the values of  $R$  are negative and hence the larger constants tend to fall off past the point  $l = 4$ . The significance of this result is not clear at present.

The experimental data on aliphatic alcohols indicate that primary alcohols are most polymerized, secondary alcohols next, and tertiary alcohols least polymerized (10) (see also figure 1).

#### XIV. THE HYDROGEN BOND AND SURFACE ENERGY

It is a well-known fact that the total surface energies of the aliphatic hydrocarbons are closely similar to the surface energies of the alkyl amines and other alkyl compounds. This has been interpreted by Langmuir, Harkins, and other workers in this field to mean that the hydrocarbon group is directed outward at the liquid surface, while the polar group is directed inward (18). In the case of an associated liquid, such as an alcohol, it is of interest to inquire into the matter of whether the surface mole-



cules form hydrogen bonds with the molecules on the interior. A simple calculation shows that the energies involved in a transfer of material from the surface to the vapor are of just the order of magnitude of the hydrogen bond energy.

When a liquid composed of spherically symmetrical molecules or atoms evaporates, the ratio of the total surface energy per mole to the latent heat of vaporization is approximately one-half. When a substance having a polar and a non-polar end evaporates, this ratio is less than one-half, because the surface energy is that required to move only the non-polar end to the surface, while in evaporation the whole molecule is moved out of the surface. In case the liquid is an associated one, this ratio may be much less than one-half (19). This may be interpreted as being due to the fact

TABLE 19

*Energy used in breaking hydrogen bonds upon vaporization from liquid surface*

TEMPERATURE	E
Methyl alcohol	
°A.	cal. per mole
363	4820
413	3870
463	2690
483	2000
503	935
Ethyl alcohol	
333	5330
383	4940
433	3670
473	2590

that in moving the molecule to the surface no hydrogen bonds need be broken, but in evaporation hydrogen bonds are broken. If it were possible to estimate the ratio of total surface energy to heat of vaporization for a material which was polar, could not form hydrogen bonds, but otherwise resembled an alcohol (in dipole moment, etc.), then any difference between this ratio and that for an alcohol could be attributed to breaking hydrogen bonds upon evaporation. As a standard material ethyl ether may be selected. The excess of energy required to move alcohol molecules from the surface to the vapor phase over that required to move ether molecules was computed from the data of Harkins and Roberts (19). The values are given in table 19. These values are of the same order of magnitude as the energy of the hydrogen bond. Some of the decrease in energy as the

temperature rises can be attributed to the fact that hydrogen bonds are broken by the thermal agitation. This is evidence for the viewpoint that hydrogen bonds are broken as the material leaves the surface, and suggests that some of the facts of surface orientation might be interpreted in terms of hydrogen bonds.

#### XV. SUMMARY

1. From both distribution ratio and molecular weight data evidence is obtained that the organic acids polymerize in non-polar solvents, largely into double molecules, and the oximes polymerize largely into low-order polymers.

2. From molecular weight data it is concluded that alcohols, acid amides, anilides, and substituted phenols polymerize into high-order polymers, and from distribution data it is known that dimers are present in non-polar solvents.

3. Molecular weight data show that —SH groups do not form hydrogen bonds to any appreciable extent and that hydroxyl groups do not form strong hydrogen bonds to sulfur atoms.

4. Molecular weight measurements indicate that a hydrogen which is used in forming a chelate ring cannot at the same time form a hydrogen bond to a neighboring molecule.

5. The abnormal vapor pressures and solubilities of ortho-substituted aromatic compounds can be explained by the concept of chelation.

6. From a consideration of molecular weights, distribution ratios, and vapor pressures it is concluded that a six-membered chelate ring is more stable than a five-membered ring, while chelation is almost inappreciable in a seven-membered ring. Chelation is sensitive to changes in bond angles and internuclear distances, as shown by the examples of the cyanophenols and sebacic acid.

7. From a consideration of molecular weights it is concluded that combination of solute and solvent occurs when hydrogen bonds can be formed between solute and solvent, and that the polymerization of solute is thereby rapidly reduced.

8. An amino type group can form strong hydrogen bonds with groups of a different type, but only weak ones with other amino groups.

9. Molecular weight data show that polymers which are held together by molecules of solvent are comparatively rare, but evidence is put forward that such combination can occur when a nitrogen atom is involved. The conclusion is not yet definite, because the data are in serious conflict in some cases.

10. Application of a theory of computing equilibrium constants to molecular weight data shows that in general the polymerization curves of the

acid amides, anilides, substituted phenols, and some alcohols lead directly to the conclusion that a succession of polymers is present, the order of the highest polymer being uncertain. Only in two or three cases is there evidence that any polymer, of the set of successive polymers, is missing.

11. The experimental data for *p*-nitrophenol in naphthalene and in *p*-dibromobenzene solution show that the successive equilibrium constants are given by

$$K_l = \frac{(l\alpha)^{l-1}}{l!}$$

Molecular weight data on benzyl alcohol and isoamyl alcohol show that the successive equilibrium constants are given by equation 3. The successive equilibrium constants for phenol in pentachloroethane are shown to be given by equation 3,  $\beta = 0$ .

12. The hypothesis that the increase in polymerization attending the entrance of a substituent into the benzene ring can be explained by an increase in the number of isomers is examined and found to be only moderately satisfactory.

13. It is shown by a consideration of surface energies and heats of vaporization that the excess of energy required to remove an alcohol molecule from the surface of liquid alcohol over that required to remove an ether molecule corresponds to breaking somewhat less than one hydrogen bond per molecule removed.

In conclusion I wish to thank Professor Linus Pauling for suggesting this review and to express my appreciation for his advice and encouragement during the course of the work. I am also indebted to Professor Roscoe G. Dickinson for the many helpful discussions that we have had, and to Marjorie Lassettre for aid in the calculations and preparation of the manuscript.

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# A SYSTEM OF STRUCTURAL RELATIONSHIPS IN PHYTOCHEMISTRY

J. ALFRED HALL<sup>1</sup>

*Forest Products Laboratory,<sup>2</sup> Forest Service, U. S. Department of Agriculture*

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## INTRODUCTION

Phytochemistry, broadly defined, embraces not only the isolation and identification of the constituents of plants, the *materia phytochemica*, but the study of the physiological processes of plant life in their relationship to the products of plant metabolism. The former phase of the science has broadened its base immensely in recent years, and the annual increment in the discovery of hitherto unknown substances in plants and in the determination of the structure of those already known is considerable. The latter phase is still, for the most part, a sealed book. There is a vast gap in our knowledge of the processes that transpire between photosynthesis and the formation of the end products of metabolism; in not one case can we surely trace the steps that intervene.

The metabolic products that are isolated from plants are for the most part stable substances, although the worker in this field is perfectly familiar with phenomena constantly encountered that prove to his satisfaction the presence of many unstable bodies. Our technic has rarely been sufficiently refined to permit the isolation of other than those substances capable of enduring the relatively drastic methods employed. These are generally the stable end products of metabolism or substances formed artificially; the intermediates escape us.

These limitations upon technic are to a large degree unavoidable, since most of the substances intervening between the carbohydrates of photosynthesis and the final products of metabolism do not, in all probability, ever exist in large concentrations. Their nature may be conceived to be a very labile one and their existence transitory. Their isolation from the living plant appears to be improbable, and their fixation in plant material prepared for examination may prove to be impossible. The comparatively

<sup>1</sup> Now Associate Director, California Forest and Range Experiment Station, Berkeley, California.

<sup>2</sup> Maintained at Madison, Wisconsin, in coöperation with the University of Wisconsin.

simple problem of the fermentation of sugar by yeasts need only be cited to indicate the difficulties in the way of a real experimental approach to the intermediate processes of metabolism in the higher plants.

The lack of experimental methods has necessitated an approach to the problem along theoretical lines in which cognizance has been taken of such organic chemical experience as could be translated into biochemical thought and due regard given to such biological experience as could be translated into organic chemical thought. Noteworthy contributions in recent years have been made by Robinson (38, 39, 40), Smedley (49), Kremers (33), Astengo (2), Francesconi (26, 27), Read (37), Emde (10, 11, 12, 13, 14, 16, 17, 18, 19), Singleton (48), Schöpf (43, 44, 45), Schmalfuss (42), and Armstrong (1).

An excellent and complete critical review of the various theories propounded concerning the relationships of the sugars and their derivatives to various classes of naturally occurring substances has been given by Bernhauer (3). A similar review, in which the important theories of Collie are adequately treated, appears in the chapter on natural syntheses in Stewart's book (50). A large mass of literature has been built around the general thesis of the biogenetics of substances occurring in higher plants, but it is not the present purpose to present a review of all the contributions. Although many of the theories advanced have had only the merit of structural possibility, they have usually embodied ideas which contributed materially to the development of the field. A generalized point of view in which a coherent explanation of phytosyntheses has been attempted is lacking.

The theory of isoprene polymerization has been advanced by many authors in explanation of the formation of such substances as the terpenes, resin acids, polyene pigments, sterols, caoutchouc, and the like (4). Perhaps it is more accurate to state that, in most cases, authors have emphasized the occurrence of the isoprene unit in various forms of condensation rather than the supposition that isoprene itself is condensed in nature to form the varied products in which this fundamental unit appears; in other words, the relationship of the "isoprene family" to isoprene is mostly assumed to be a formal one, and not necessarily a biogenetic one. Wagner-Jauregg (51) accomplished the syntheses of the olefinic terpenes and their relatives under the mildest conditions yet observed, which still fall far short of realizing biological conditions. If a synthesis of terpenes could be carried out from isoprene under biologically probable conditions, the explanation of the formation of isoprene itself would still be wanting. The same reasoning may be applied to the idea of  $\beta$ -methylcrotonaldehyde as the fundamental unit of this family of compounds (20). Further, the structural relationship of the isoprene group to other associated groups would still be lacking.

While the recurrence of the isoprene unit in the structures of the more stable end products of plant metabolism has been most striking, especially in its relation to the elucidation of structures of many complex and baffling substances, many other structural regularities in plant products are discernible. Armstrong (1) has pointed out a number of them, and Emde (13, 14, 15, 17, 18) may well be said to have formulated a "reconstructive biochemistry" upon the basis of such regularities.

Schöpf (43, 44, 45) has defined a technic and has carried out most interesting investigations in the synthesis of the *Angostura* and other alkaloids under physiological conditions from materials suggested largely as a result of "reconstructive" reasoning. According to Schöpf, the formation of natural substances in the living cell may be of three types: In the first, the cell may have an enzymatic system designed for the highly specific synthesis of a certain substance. An example is the formation of starch in the assimilation of carbon dioxide. The second type is enzymatic but general, that is, the result of processes of general application catalyzed by enzymes, e.g., hydrogenation, dehydrogenation, and decarboxylation. The third case is of the synthesis of natural substances, or stages of such synthesis, without the action of enzymes. Such cases are characterized by the formation in the growth of the cell of organic substances so reactive that they, upon contact in the cell, yield isolable products which are, in effect, chance products, or stages in the production of such.

The technic or reasoning process of Emde and Schöpf, used also in part previously (28) by the author of the present paper, starts with the final product of metabolism, the structure of which must be known. At the other end of the road, serving as guideposts, stand the natural hexoses and their closer relatives. One must work backward step by step toward this beginning, with only such guidance as is afforded by our comparatively meagre information concerning reactions under biological conditions. The intermediate products may never be any more apparent than are those in an ordinary alcoholic fermentation.

Schöpf makes the important reservation that no broad conclusions as to precursors can be drawn from the constitution of an individual substance. However, if one has a large number of natural products of related constitution, as is the case today in many groups, there is possible a sort of "comparative anatomy" of analogies and regularities in make-up, from which one can draw probable conclusions concerning the precursors. Also, an important method of testing conclusions as to biogenetic relationships is the systematic survey of the occurrence in plants of substances supposed to be biogenetically related. This method must, however, be used with great care, since it is apt to mislead the investigator. The difficulty arises from the fact that often where substances may appear to be biogenetically related and perhaps derivable from one another, in



fact they are more probably derived from a common precursor in which the necessary configuration has been established, but have followed different routes in subsequent elaboration. In most groups, accurate knowledge of occurrences and cooccurrences is too limited as yet to warrant the use of this method.

#### THE KEY POSITION OF QUINIC ACID

A case in point may well be the relationship existing structurally between quinic acid and citric acid, which will be developed in the subsequent argument. The two acids occur widely, but those plants noted for their quinic acid content are not producers of citric acid, and *vice versa*. In spite of the clear-cut oxidation of quinic acid to citric acid accomplished by Fischer and Dangschat (24), it seems more probable that citric acid and quinic acid are derived from common or analogous precursors than that citric acid is derived directly from quinic acid. Clutterbuck (7) points out that the direct derivation of citric acid, according to

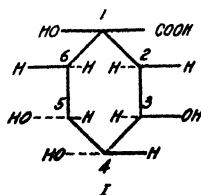


FIG. 1. Quinic acid

Emde's suggested equation in which quinic acid is assumed to be an intermediate, can give a theoretical yield of only 56 per cent, as against attainable yields of 87 per cent in *Aspergillus* fermentations.

An interesting example, however, of the controlling influence that can be exerted by "reconstructive" reasoning is afforded by the history of the structural proof for quinic acid. Emde (15) deduced the correct formula for this substance upon purely theoretical grounds. Karrer (31) arrived at a different conclusion from excellent experimental evidence. Fischer and Dangschat (22, 23) were able to show Karrer's error and substantiate Emde's original formula. The point is that quinic acid could not be intelligibly fitted into a biogenetic scheme until its structure was known, and the biogenetic scheme afforded an excellent check upon the structure deduced from purely organic chemical reasoning.

The question of the biogenetic origin of quinic acid is an important one from several points of view. It may well be said to occupy a key position in any scheme of biogenetic development. Its structure, as elucidated by Fischer and Dangschat, is shown in figure 1. It contains a carboxyl group

attached to a carbon atom which carries a hydroxyl group, this carbon atom being joined to two methylene groups. The origin of the carboxyl group in this particular situation is very important, as is the origin of the two methylene groups, for there is present in this configuration the ubiquitous isopropyl grouping. Perhaps of greater importance is the spatial arrangement on carbon atoms 3, 4, and 5 of the ring. Inspection shows that the arrangement is the same as that on carbon atoms 3, 4, and 5 of the naturally occurring hexoses *d*-glucose, *d*-mannose, and *d*-fructose as well as the *l*-varieties, when all are written in the acyclic form.

#### ORIGIN OF THE —COOH GROUP IN PLANT SUBSTANCES

Until the photosynthesis in plants of other compounds than the sugars has been demonstrated, phytosyntheses must be assumed to start from the sugars produced by photosynthesis. In this case only oxidative or

dismutative processes operating upon  $\text{—CH}_2\text{OH}$ ,  $\text{=CHOH}$ ,  $\text{—C} \begin{smallmatrix} \text{H} \\ \diagup \\ \text{O} \end{smallmatrix}$ , or

$\text{=C=O}$  can produce  $\text{—COOH}$ . We know that linkages between hexose molecules can be glycosidal linkages, 1-4 and 1-6 in the cases of reducing disaccharides, of which the 1-4 linkage is found in the important cellobiose and maltose. We may also have the 1-2 linkage, as in sucrose. In these cases we can conceive of the degradation of one of the chains giving rise to a  $\text{—COOH}$  group as a final result. They may also give rise to methoxyl, ethoxyl, or ethylene oxide groups, which may be formed according to the ingenious scheme advanced by Browne and Phillips (5). For present purposes the fundamental conception of the carboxyl groups as a product of the oxidative or dismutative degradation of a chain is sufficient, but the additional concept of carbon-to-carbon linkages between hexose chains, or residues of such chains, is helpful. We have no certain knowledge of the existence of such linkages, but we have practically no knowledge of the nature of the carbohydrate linkages in a vast number of hemicelluloses, pectins, gums, and the like in which carboxyl groups are present.

In the uronic acids, the presence of a carboxyl group on carbon atom 6 can be conceived of as the product of the oxidation of the terminal  $\text{—CH}_2\text{OH}$  group. The apparent non-existence of free uronic acids in plants indicates that this operation is not carried out on uncombined hexose molecules. Aside from the oxidation of a biose in which a terminal carboxyl is formed on one of the chains, there are only two alternatives: (a) the carboxyl on the second chain arose after its combination with hexose or other molecules by oxidation on carbon atom 6 alone; (b) it arose as a residuum of the oxidation of a hexose or other chain linked by a carbon-carbon bond to carbon atom 6 of the second chain. In view of the

relatively great difficulty in effecting the oxidation of carbon atom 6 *in vitro*, and its impossibility unless adequate protection is afforded the rest of the chain, and in view of the relative ease of biochemical oxidation starting at, e.g., carbon atom 2 of the fructose chain, it seems more logical to adopt the second alternative, viz., the carboxyl group of the uronic acids may arise from the oxidative degradation of a hexose or other chain (or chains) attached to carbon atom 6 by a carbon-to-carbon bond. Such a degradation may be roughly formulated as in figure 2.

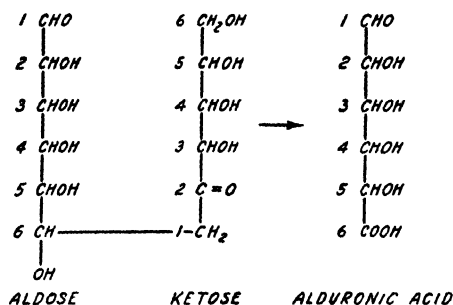


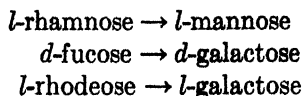
FIG. 2. Formation of carboxyl group

It is clear that many other types of union can give rise to terminal  $\text{—COOH}$  groups, but in most cases the more logical assumptions are based upon carbon-carbon linkages between atoms forming parts of carbohydrate chains.

#### ORIGIN OF THE TERMINAL METHYL GROUP AND METHYLENE GROUP

A similar line of thought accounts for the terminal methyl group better than does the postulation of a rather drastic process of reduction. The development of  $\text{—COOH}$ , for example, on carbon atom 2 of the fructose chain may be followed by decarboxylation and the formation of  $\text{—CH}_3$  at carbon atom 1 (figure 3a), or the  $\text{—CH}_3$  may appear at carbon atom 6 of the aldose chain (figure 3b). A similar action taking place on a carbon-carbon bond within a hexose chain may give rise to  $\text{—CH}_2$  (figure 3c).

The existence of the desoxy sugars may be explained as well in this manner as by a dismutational action. The fact that the methylpentoses whose structures are known are related in a configurational sense to the hexoses in the following way,



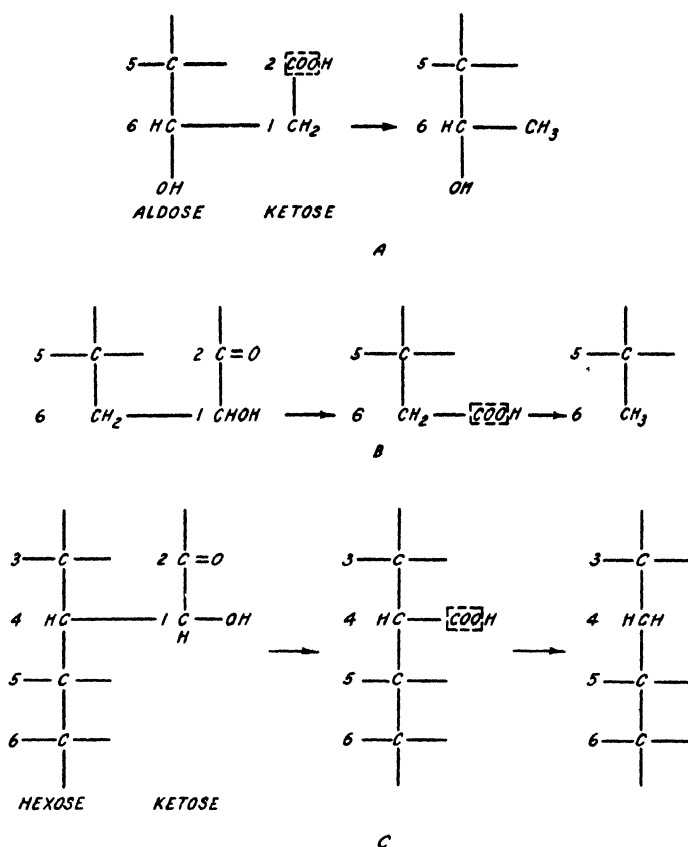


FIG. 3. Formation of methyl and methylene groups

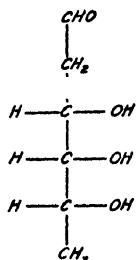


FIG. 4. Digitoxose

and the apparent non-occurrence of *l*-mannose and *l*-galactose in plants may be related to the peculiar configuration of digitoxose (figure 4) an-

nounced by Micheel (36), in the sense that these compounds arise, not from single hexose chains by dismutational processes, but from an original complex of perhaps several hexose chains or residues in which one or more carbon-carbon bonds are involved.

#### THE FUNDAMENTAL UNITY OF PLANT SUBSTANCES

The recurrence of the same or essentially similar structural units among plant substances, and the many times repeated coöccurrence of many of these units furnish a basis for the belief that the end products which we examine, although structurally quite dissimilar, may have arisen from common precursors, the latter stages of structural elaboration having taken place under slightly dissimilar conditions. Structural relationships in plant substances often do not appear in the conventional classifications of most organic and biochemical books. They must usually be developed by "reconstructive" methods. In the following discussion the dominant thought has been to demonstrate the possible common origin of widely

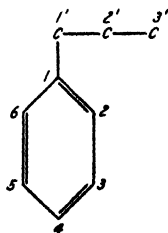
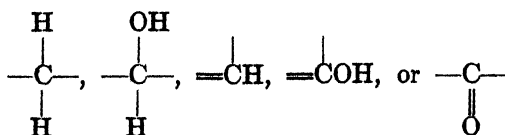


FIG. 5. Common  $C_6-C_3$  form

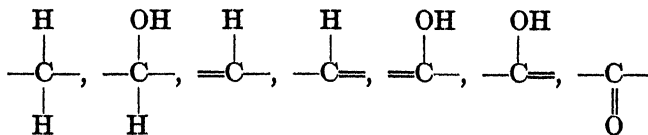
diversified compounds occurring in higher plants, that origin being the usually occurring hexose sugars.

The special products of metabolism of the fungi have not been discussed, since it was felt that the new point of view could be developed more freely if not limited by older ideas based upon theories and observations in connection with fermentation phenomena.

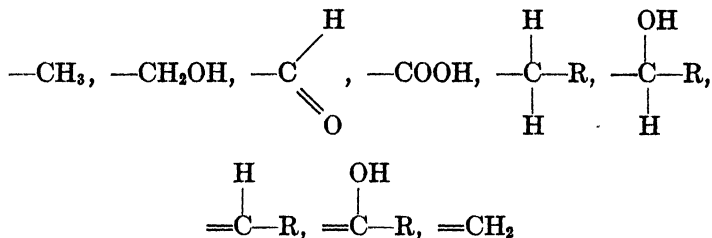
Two principal types of naturally occurring molecules will be treated,—the "isoprene family" and the vast group in which the  $C_6C_3$  grouping predominates. As Armstrong (1) has pointed out, the natural aromatic compounds may be conveniently classified, first, according to the length and state of oxidation of the side chain, and second, by the number of hydroxyl groups in the nucleus. The simplest types are as in figure 5, where theoretically  $C_7$  may be:



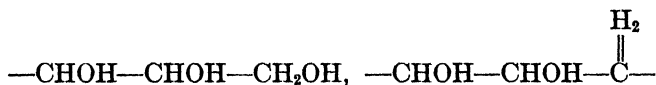
C<sub>3</sub> may be:



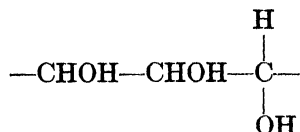
C<sub>3</sub> may be:



Not all of the above configurations have been observed in natural products, but examples are known of the major part of them. It follows that, in a formal development, the assumption is necessary that these configurations can be derived from



or from



by the application of the ordinary oxidation and oxido-reduction mechanisms or the processes postulated for the formation of  $-\text{CH}_2$  and  $-\text{CH}_3$ . The position and number of hydroxyls in the nucleus will be developed later.

A further assumption, fundamental to the conceptions to be developed, is in disagreement with the idea generally held that most plant products are formed by the union of small units resulting from sugar degradation. Collie (8) suggested that after molecules of great complexity have been built up from the product or products of photosynthesis, these undergo degradation to simpler compounds, and that conditions of slightly varying acidity or alkalinity may determine the actual constitutions of the final products. Clutterbuck (7) suggested that polysaccharides are intermediates in the biological syntheses of certain acids produced by molds.

He also brought forward the idea that this may be of rather general application. It may be considered that in regions of photosynthetic activity energy is consumed in the synthesis of these complexes, which in turn furnish the required energy to carry out the subsequent anoxidative processes of growth and metabolism. *The resulting end products, which can be isolated, may be the results of configurations already established by the mode of union in the original complexes.*

#### DERIVATION OF THE CINNAMIC ACID SERIES

The underlying configuration suggested by the known structure of cinnamic acid (figure 6) is found in the metasaccharonic type of acid of Kiliani (figure 7) (32). For purposes of formal development it is necessary to consider probable mechanisms for the formation of this or similar configurations in the plant. According to the argument developed above, relative

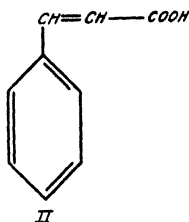


FIG. 6

FIG. 6. Cinnamic acid

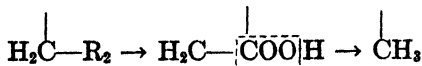


FIG. 7

FIG. 7. Metasaccharonic acid

to the arising of  $\text{—COOH}$  and  $\text{—CH}_2$  groups *in vivo*, it may be considered that  $\text{—C—C—}$  linkages would exist on carbon atoms 3 and 6 of the hexose chain. The  $\text{—CHO}$  group at carbon atom 1 is regarded as oxidized to the carboxyl group by known biological mechanisms. The derivation of III, the general metasaccharonic configuration, from an aldohexose, might then follow as in figure 8. Carbon atom 1 may be glycosidally linked, as may  $\text{C}_4$  and  $\text{C}_6$ .  $\text{R}_1$  might be on  $\text{C}_4$ .

The situation on  $\text{C}_6$  might be  $\text{HC—R}_2$ , in which case the process indicated might form a terminal methyl group:



In this case, not a representative of the cinnamic acid series, but a member of the series with the side chain  $-\text{CH}=\text{CHCH}_3$  would result.

Cinnamic acid itself can be derived by joining two molecules of III, as indicated in figure 9. The relationship between cinnamic acid and benzyl

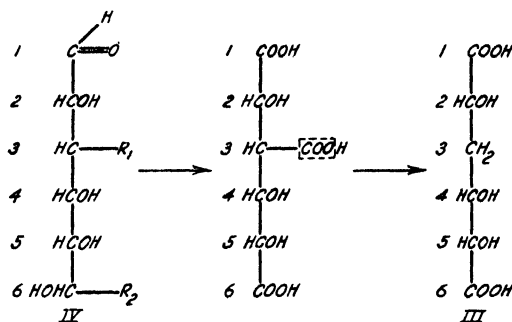


FIG. 8. Derivation of metasaccharonic acid

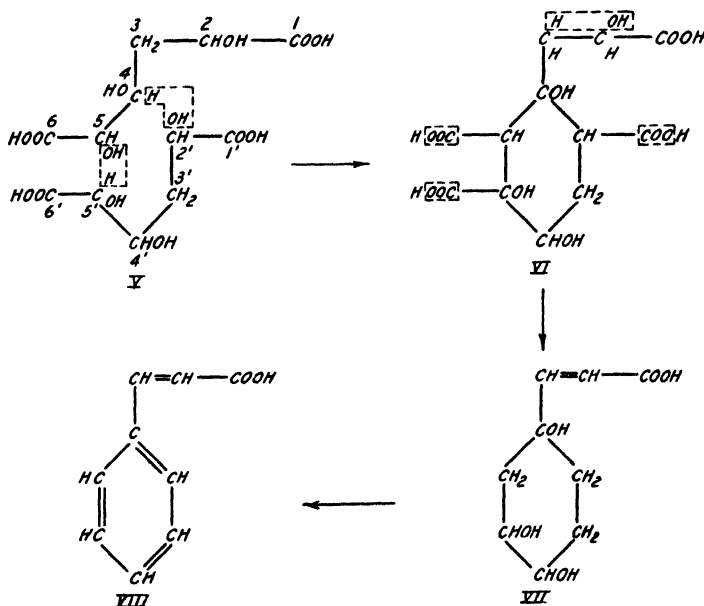


FIG. 9. Derivation of cinnamic acid

alcohol, benzaldehyde, and benzoic acid need only be suggested here. Clearly the side chain, formed from carbon atoms 1, 2, and 3 (or 4, 5, and 6), may be conceived of as being oxidized at any stage after that shown in formula V. As indicated above, the allyl and propenyl side chains may



be conceived of as arising because of a special situation at  $C_1$  of the upper chain, which, if  $R_1$  in formula IV were on  $C_4$ , might just as well be  $C_6$  of the original hexose chain.

The condensation shown as taking place between carbon atoms 5 and 5' and 4 and 2' may take place in three other ways, depending upon the source of  $-H$  and  $-OH$ , but the result is the same in all cases, and subsequent dehydration within the nucleus results in the benzene ring.

It is important to apprehend that the condensation shown is conceived of as taking place not necessarily between two molecules of a metasaccharonic acid but *between two hexose molecules so joined with other chains that the metasaccharonic configuration is produced by degradation of the original condensed, but much larger, molecule. Nothing is specified as to the order in which these events may transpire.* For formal development, subsequently, the finally developed metasaccharonic type of molecule will be used. The limitations of graphic presentation prevent the use of the basic conception of the large molecule. In effect, carboxyl groups in subsequent developments represent points of union for chains.

#### THE MONOHYDROXYCINNAMIC ACID SERIES

In the formal development of the various monohydroxycinnamic acids (figure 10) it is necessary to use one molecule of III as derived above, and one molecule of dicarboxylic sugar acid (IX). The formation of the two terminal carboxyls in the case of the latter may be conceived of as having arisen in the manner postulated under the derivation of cinnamic acid. In this formal development no regard need be had for the stereochemical arrangement on the remaining carbon atoms, although it is clear that this may play an important part in directing the manner in which condensations and dehydrations may take place by the elimination of  $-H$  from one carbon atom and  $-OH$  from another.

Although all three of the monohydroxycinnamic acids are possible under this derivation, only the ortho and para forms have been found in nature. A few occurrences of *m*-hydroxybenzaldehyde indicate the probability that the meta form exists. The ortho variety is, of course, *o*-coumaric acid, and derived from it, or along with it in the same manner as shown in the relationships between cinnamic acid and benzoic acid, are saligenin, salicylic aldehyde, and salicylic acid.

The para form is found mostly in combinations in which the side chain is in a more highly oxidized form, as in apigenin, scutellarin, genkwanin, and campherol, although the free *p*-coumaric acid has been reported a number of times.

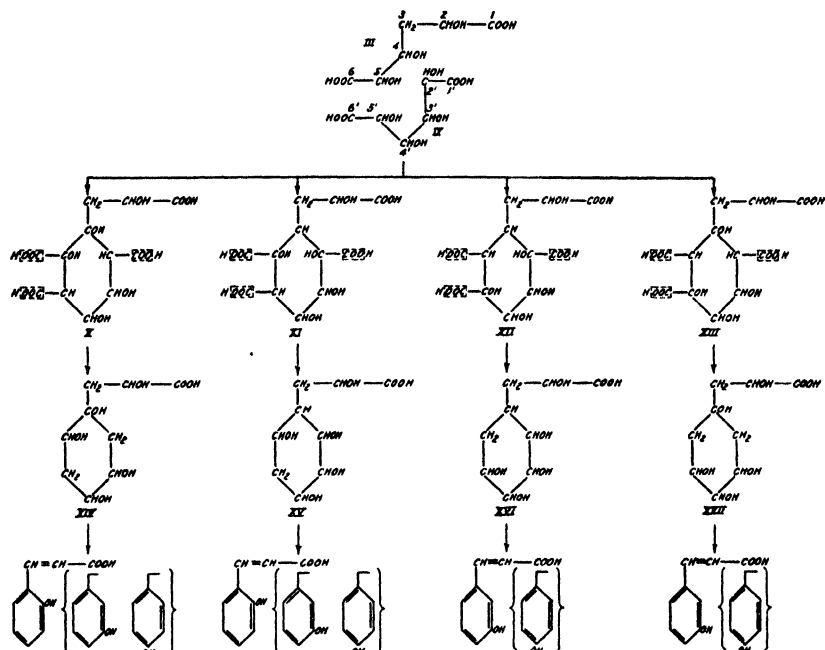


FIG. 10. Derivation of monohydroxycinnamic acids

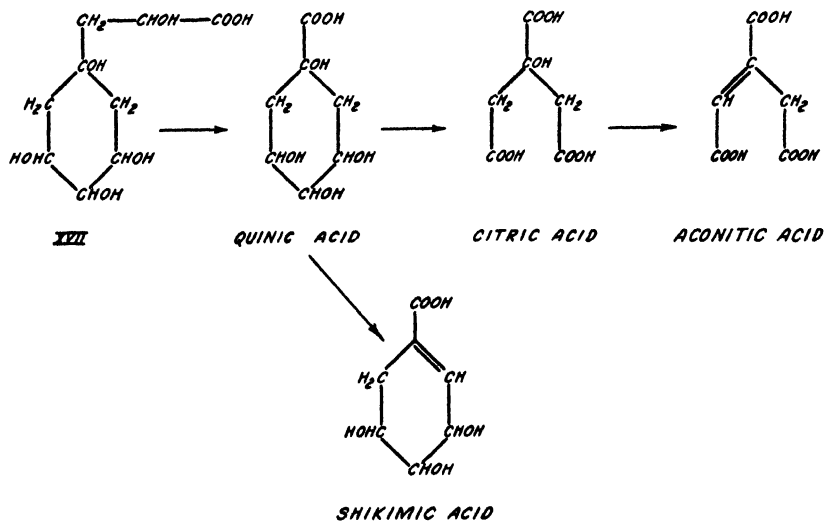


FIG. 11. The quinic acid series

## DERIVATION OF QUINIC ACID

A slight variation in the course of the operations outlined in the derivation of the monohydroxy acids leads to quinic acid as the principal representative of a family of several acids. For convenience, the derivation can be carried out from formula XVII simply by oxidizing the side chain to  $\text{—COOH}$  (figure 11). The relationship existing between quinic acid and the following acids was pointed out by Emde in 1931 (13), although at that time he seems to have abandoned his own idea of the structure of quinic acid and shikimic acid in favor of Karrer's formula (31). The relationship is much more apparent when based on Fischer's formula for quinic acid (23). Again it must be emphasized that the relationship shown is only a formal one and does not postulate the derivation in straightforward fashion as shown. It is much more probable that the course of subsequent oxidative degradation is determined by the situation existing in stage XIII with respect to combinations on extracyclic carbon atoms. In stage XIII the necessary arrangement exists to cause the degradation to take any of several courses under different conditions. Perhaps of considerable importance in lending some weight to the arrangement here postulated is the fact, already pointed out, that the stereochemical configuration on carbon atoms 3, 4, and 5 of XIII, and consequently, of quinic acid, is the same as that on carbon atoms 3, 4, and 5 of glucose, fructose, and mannose.

## DERIVATION OF THE TERPENES

The biogenetic origin of the terpenes is a part of the whole problem of the origin of branched-chain compounds, as well as those containing six-membered rings and side chains of varying length.

It is of considerable interest to find that the terpenes may be closely related biogenetically, according to the present scheme, to the foregoing substances with which they appear to be also closely associated in occurrence. In fact, it was a search for a fundamental reason for the existence of the relationships shown by the author (28) to exist among the terpenes that led to the development of the system being discussed.

The terpene derivation must be done in two separate stages, which lead to two slightly different hypothetical "half-molecules" closely related to acetonedicarboxylic acid. These are finally united to give the desired configurations.

To develop the first half, we must refer to XVII (or XIII). If it be assumed now that the side chain is stabilized and oxidation takes place in the cycle, the result is XVIII (figure 12). It will be seen that the process is the same as that employed in the derivation of citric acid, except that the side chain has remained intact.

In the development of the second hypothetical terpene precursor

(figure 13), it is necessary to go further back to the original union of III and IX under "derivation of the monohydroxycinnamic acid series" (figure 10), and join them in a little different fashion. The orientation of III with respect to IX is simply reversed. XX is the desired other half of the terpene derivation. For present purposes, let XVIII be A and XX

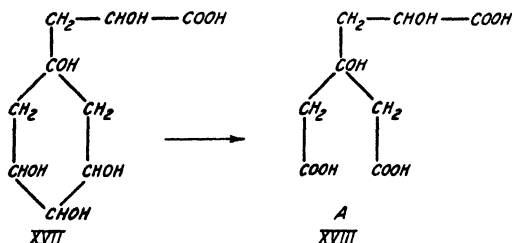


FIG. 12. A in terpene derivation

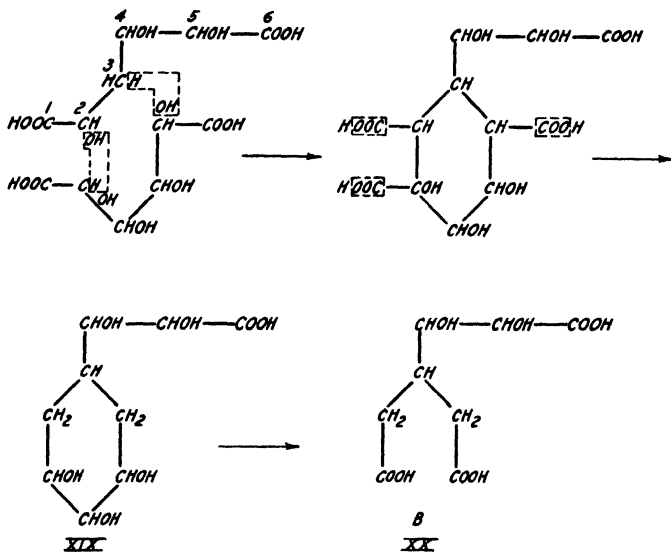


FIG. 13. B in terpene derivation

be B. There are clearly four combinations possible: A, B; A, A; B, B; and B, A. The combinations can be effected as shown in figure 14.

An alternative derivation of certain terpenes, probably more nearly what occurs, is shown in figure 15. If all the possible combinations of XVII and XIX are condensed as shown, all the terpenes are possible.

The four glycerols derived in figure 14 are identical with the ones postulated by the author (28) as underlying all the terpenes. The glycols

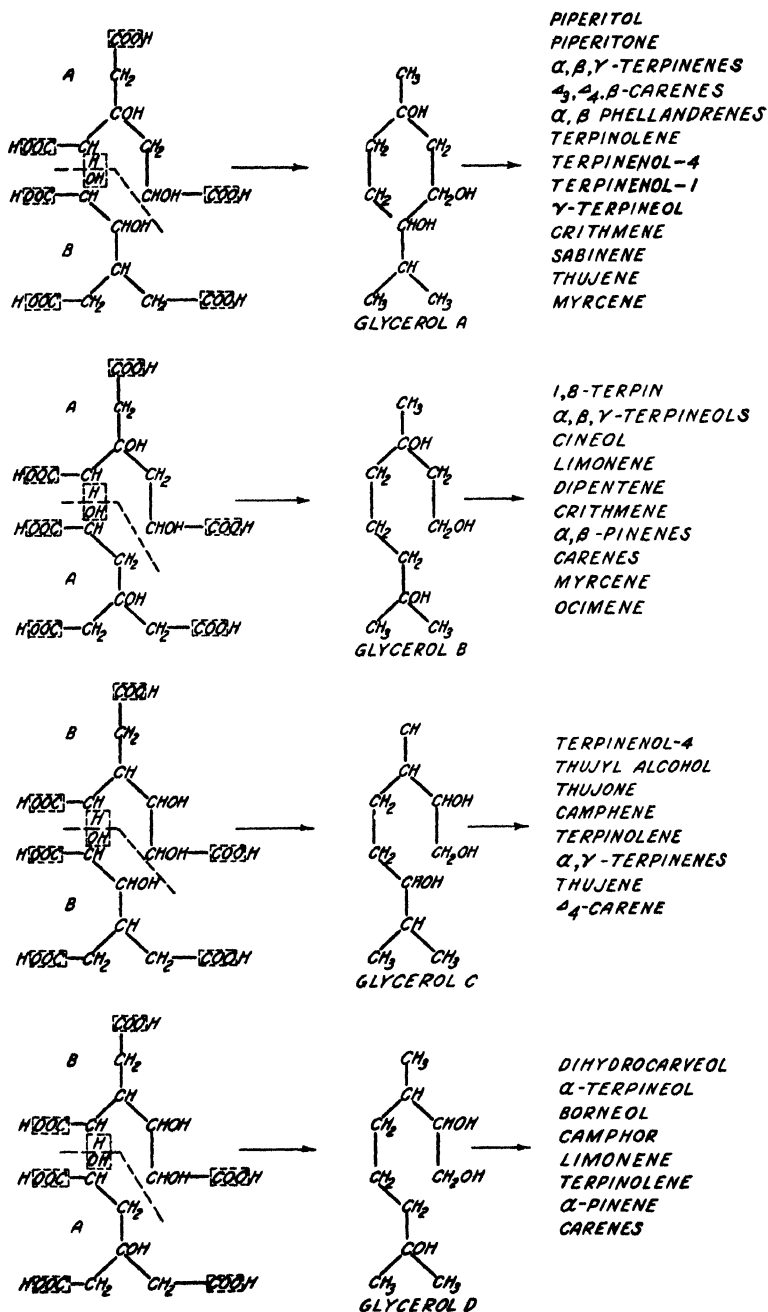


FIG. 14. Derivation of terpenes

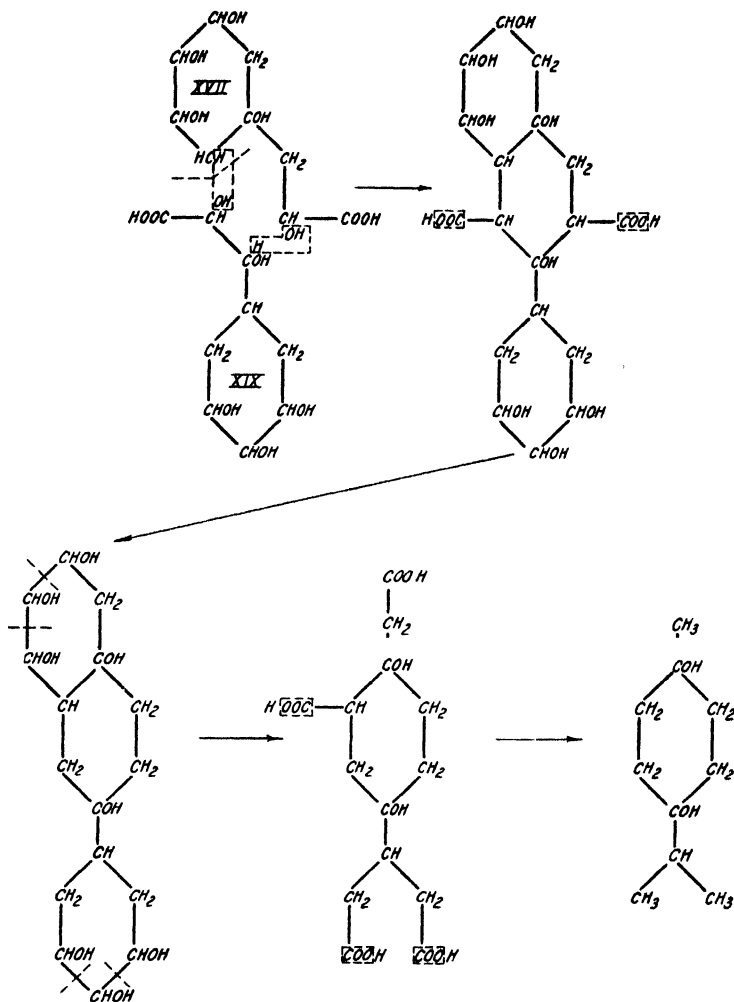


FIG. 15. Alternative derivation of the phellandrene family

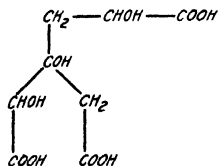


FIG. 16. Configuration C in vitamin A

derived according to figure 15 are those shown as possibly derived from the glycerols. The author showed by means of a sort of census of coöccur-

rences that the associations of the various terpenes and terpene alcohols in plants conformed very closely to that required by their postulated<sup>1</sup> origin.

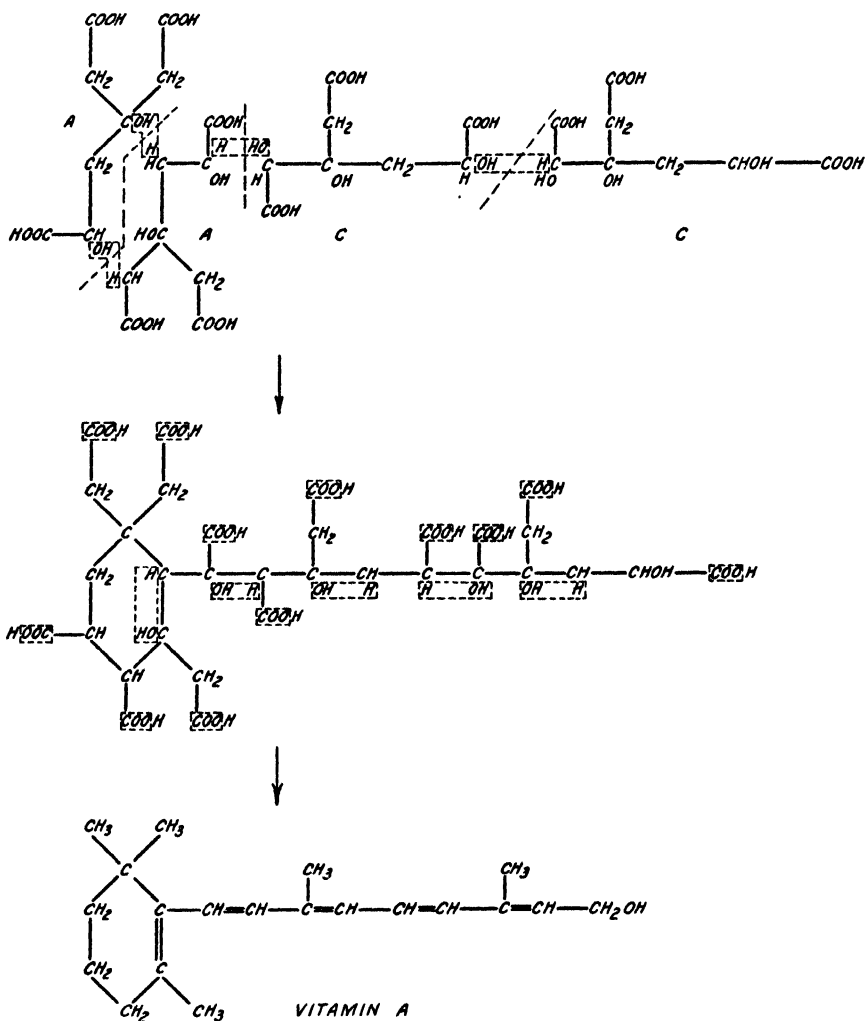


FIG. 17. Derivation of vitamin A

It will be observed that A and B are closely related to isoprene. There seems to be every reason to believe that by similar structural reasoning the entire "isoprene family" can be brought into harmony with the system developed. A few examples can be developed here, e.g., the derivation of

vitamin A according to the formula of Karrer (21, 30). Here will be utilized the progenitor, A, of the terpene derivation and a similar configuration, C (figure 16), which can be derived by a similar process from X or XIV. They may be arranged as in figure 17 to give a derivation of vitamin A.

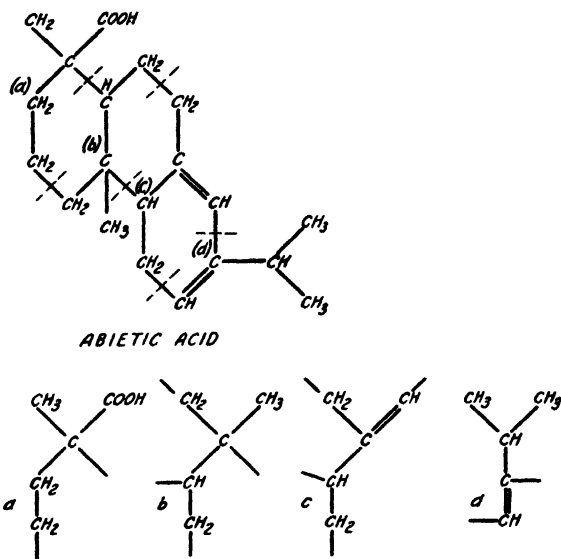


FIG. 18. Abietic acid and its subdivision into parts a, b, c, and d

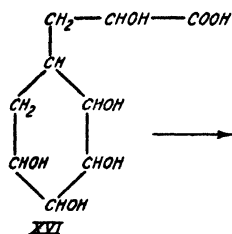


FIG. 19

FIG. 19. Derivation of part a in abietic acid

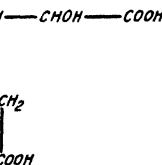
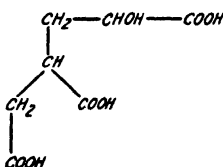


FIG. 20

FIG. 20. Derivation of part b in abietic acid

#### DERIVATION OF ABIETIC ACID

According to Ruzicka (41) abietic acid has the formula shown in figure 18. It may be broken up into the four five-carbon atom fragments a, b, c, and d. Fragment a can be derived from XVI (figure 19); b is derived from XX (figure 20); c is derived from two hexose molecules or two dicarboxylic



sugar acids (figure 21); and d is the same as b. The full derivation of abietic acid is shown in figure 22.

Space limitation prevents the carrying out here of further derivations in the "isoprene group," but the methods used seem to be capable of wide extension.

The mysterious origin of the branched-chain sugar, apiose, is explainable in a similar manner in figure 23 and thus harmonized with the derivation of the terpenes. Stewart<sup>3</sup> showed a possible derivation of the terpenes from apiose, the synthesis of which he postulated as arising by formaldehyde condensation.

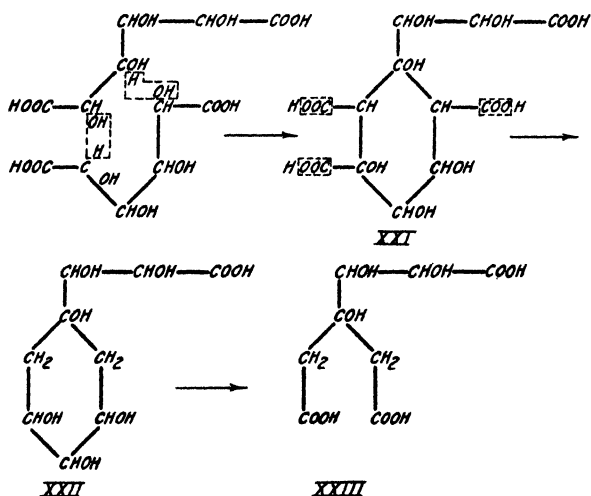


FIG. 21. Derivation of part c in abietic acid

#### ALIPHATIC HYDROCARBONS AND RELATED SUBSTANCES

The problem of the relation of *n*-heptane to the terpene system of synthesis is an interesting one. Heptane occurs in the oleoresinous secretions from *Pinus jeffreyi* and *Pinus sabiniana*, as well as in *Pseudotsuga macrocarpa*, in a manner exactly analogous to the occurrence of the terpenes, associated with resin acids of the abietic type which are evidently very closely related to, if not entirely identical with, the resin acids of many other pine oleoresins in which the volatile portion consists of terpenes. It is at least very suggestive to note that the *n*-heptane chain can be derived in a manner analogous to that in which the formation of the terpenes and resin acids was postulated.

If XX, which was B of the terpene derivation, be combined with

<sup>3</sup> Reference 50, Vol. 2, p. 292.

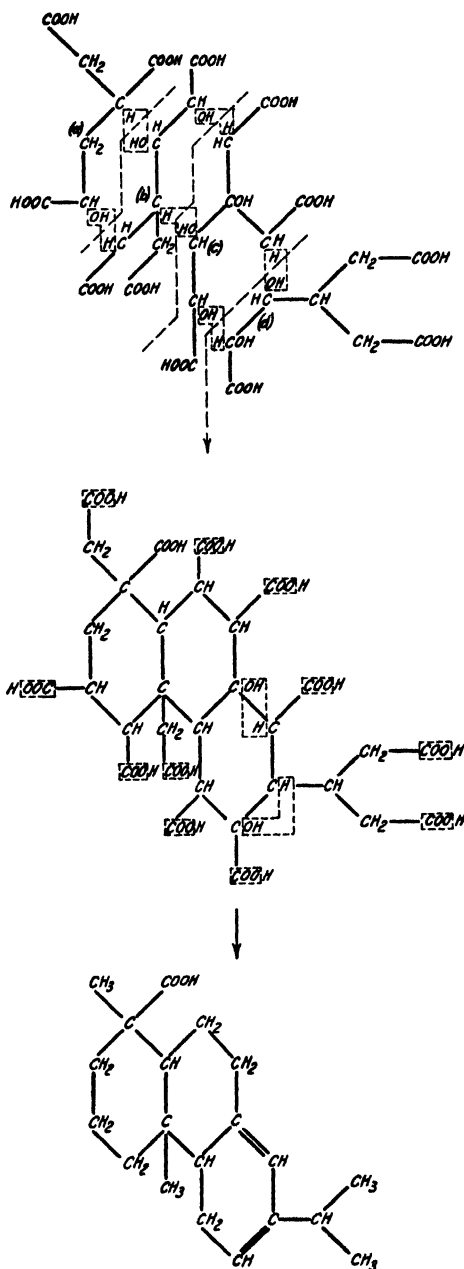


FIG. 22. Derivation of abietic acid

fragment a of the abietic acid derivation, which arose from XVI, the sequence shown in figure 24 seems possible.

With few exceptions, there appears to be a rough sort of periodicity of four in the occurrence of normal paraffins in higher plants. According to

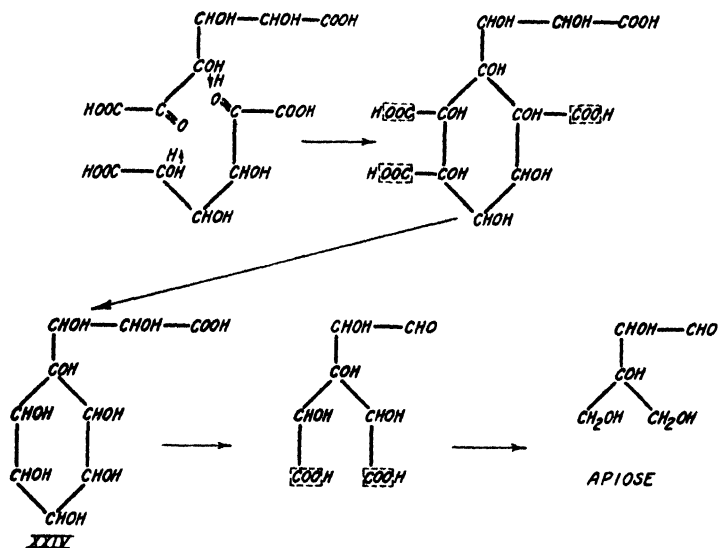


FIG. 23. Derivation of apiose

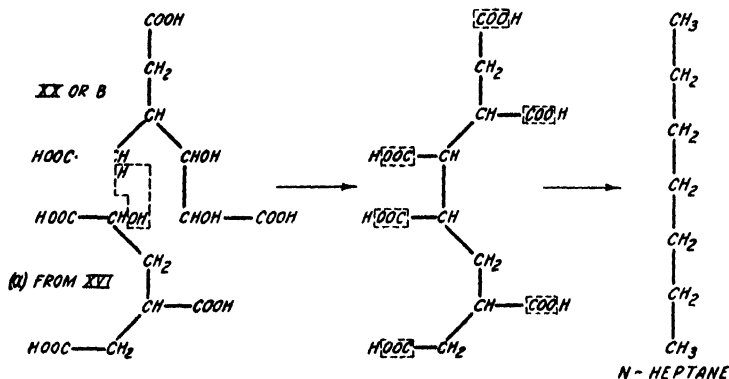


FIG. 24. Derivation of *n*-heptane

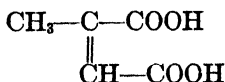
Chibnall and his coworkers (6) the usual plant and insect waxes may contain odd numbers of carbon atoms up to  $C_{37}$ . They list recorded occurrences, subject to earlier limitations of technic in identification, up to the year 1930 as follows: *n*-heptane, 7; *n*-pentadecane, 3; *n*-hexadecane, 1;

*n*-eicosane, 1; *n*-heneicosane, 1; *n*-docosane, 3; *n*-tricosane, 3; *n*-pentacosane, 1; *n*-hexacosane, 1; *n*-heptacosane, 11; *n*-octacosane, 1; *n*-nonacosane, 2; *n*-triacontane, 19; *n*-hentriacontane, 26; *n*-dotriacontane, 2; and *n*-pentatriacontane, 15. To these should be added at least two occurrences of *n*-undecane in *Pinus excelsa* (47) and *Pinus monticola* (25) and a suspected occurrence in *Pinus lambertiana* (46). Marion (35) reports the occurrence of *n*-nonane in *Sarothra gentianoides* L.

In the light of the investigations of Chibnall's school, it seems highly probable that many of the reported occurrences of normal hydrocarbons with even numbers of carbon atoms are in error, and that many other reported occurrences of pure hydrocarbons of high molecular weight really dealt with mixtures. It is a little suggestive that the curve of occurrences rises so abruptly at C<sub>27</sub>, C<sub>31</sub>, and C<sub>35</sub>. The nineteen reported occurrences of C<sub>30</sub> hydrocarbons in all probability dealt with mixtures. However, Chibnall and his coworkers have abundantly proven the occurrence of C<sub>25</sub>, C<sub>29</sub>, and C<sub>33</sub> hydrocarbons, so that there is obviously no rigid periodicity of four; if it exists it is superimposed upon a periodicity of two.

It is easy to see how, starting with C<sub>7</sub>, increments of four carbon atoms, derived perhaps from a (figure 24) or perhaps from other similar configurations, would build up in periods of four. If the tertiary carbon atom in a carries a hydroxyl group instead of hydrogen, the increment might be reduced to two.

When the above reasoning is applied to the saturated straight-chain dicarboxylic acids, no such regularity appears. The derivation of *n*-heptane above could give azelaic acid if the terminal carboxyl groups were retained. We have, however, higher acids as follows: sebacic (C<sub>10</sub>), thapsic (C<sub>16</sub>), rocellic (C<sub>17</sub>), japanic (C<sub>21</sub>), *n*-eicosanedicarboxylic acid (C<sub>22</sub>), *n*-heneicosanedicarboxylic acid (C<sub>23</sub>). No unsaturated dicarboxylic acids are known in plants above mesaconic acid:



With a single exception, phloionic acid, C<sub>16</sub>H<sub>30</sub>(OH)<sub>2</sub>(COOH)<sub>2</sub>, no higher hydroxydicarboxylic acids have been found.

From condensations of the various "half-molecules" in the manner used in the derivation of *n*-heptane, almost any conceivable situation with regard to hydroxyl groups in the chain can arise. It seems at least possible that herein lies an explanation of the formation of the saturated dicarboxylic acids, the saturated monocarboxylic acids, the unsaturated monocarboxylic acids, the aliphatic alcohols and ketones, and the hydrocarbons, in all of which a straight carbon chain is present. The relatively few examples utilized here can certainly be greatly increased in number.

The formation of a particular compound or class of compounds may be determined by the situation in the vicinity of the terminal carboxyls, ease of decarboxylation, susceptibility to further oxidation, or relative stability in its chemical environment. The occurrence of double bonds, hydroxyls, or carbonyls within the chain may be determined by the position of hydroxyls and side chains in the original condensed compound.

It must be admitted that the biogenesis of the whole field of aliphatic hydrocarbons, alcohols, aldehydes, and acids is less satisfactorily explained by the general system here developed than are the other fields treated. On the other hand, they can be fitted into the general scheme, although with less assurance than in the other cases. We are not yet in full possession of information with respect to the regularities in the position of double bonds in the straight-chain olefinic monocarboxylic acids. A full consideration of the known structures now available does not reveal consistent regularities at all.

Evidence is not wanting of the validity of the application to fat synthesis of Collie's theory of successive dehydration and reverse hydration on carbohydrates.<sup>4</sup>

#### DERIVATION OF THE DIHYDROXYCINNAMIC ACID SERIES

Members of this series have not been found free in nature. However, the following compounds are found, upon inspection, to contain the carbon skeleton of the series, with the side chain in various stages of oxidation: coniferyl alcohol, cubebin, caffeic acid, umbelliferone, luteolin, morin, quercetin, gossypetin, fisetin, and quercetagenin. Protocatechuic alcohol, protocatechuic aldehyde, and protocatechuic acid are conceived to be related to this series as benzyl alcohol, benzaldehyde, and benzoic acid are to the cinnamic acid series. It is significant that the representatives of the 3,4-dihydroxy series predominate; a few occurrences only of the 2,4 series are reported; a single occurrence of 2-hydroxy-6-methoxybenzoic acid suggests the occurrence of members of the 2,6 series; the 2,3, the 3,6, and the 3,5 series are all lacking.

The 3,4 representatives are of great importance in numerous glucosides, especially of the  $\gamma$ -pyrone family and the anthocyanins.

The required configuration is given by the union of one molecule of metasaccharonic acid with a molecule of an  $\alpha$ -ketodicarboxylic acid which may be conceived as arising from the oxidation of a ketose chain on which radicals were attached to carbon atoms 1 and 6, or from an aldose chain similarly connected, by oxidation on C<sub>6</sub> in the usual manner leading to acids like 5-ketogluconic acid. Thus, the necessary underlying chains are an aldose and a ketose, or two aldoses (figure 25).

<sup>4</sup> Reference 50, p. 294.

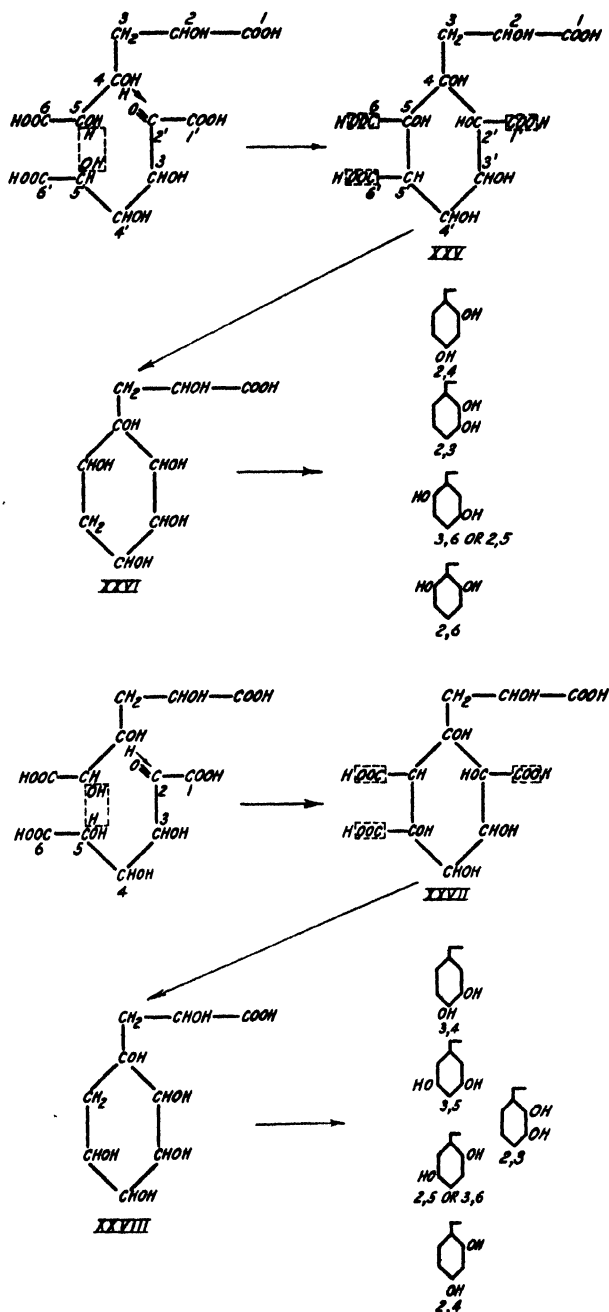


FIG. 25. Derivation of the dihydroxycinnamic acid series

In accounting for the occurrence of only the 2,4- and the 3,4-dihydroxy compounds, the situation in XXV must be considered. Assume that carbon atom 4' is united glycosidally to R. Then the derivation may proceed as in figure 26. If dehydration goes as in XXX, a 2,4 product results; if as in XXXI, a 3,4 product is formed.

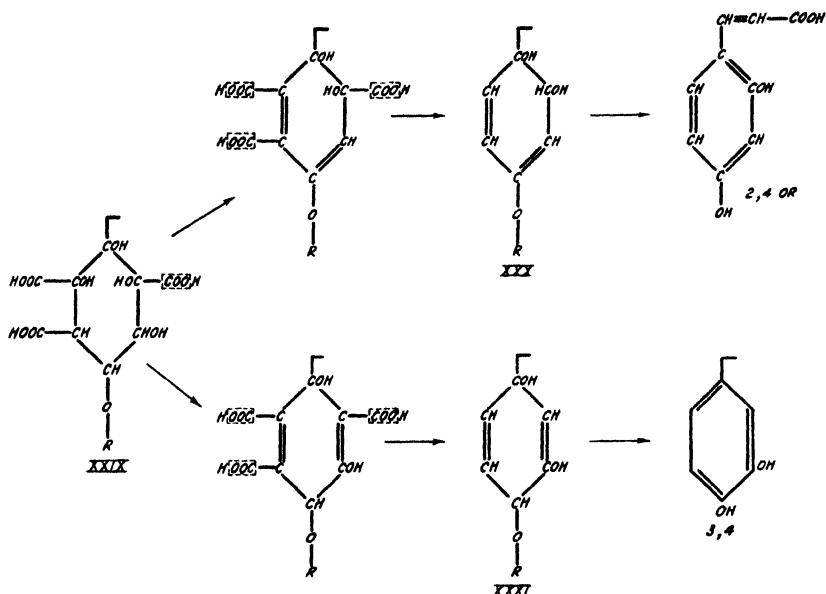


FIG. 26. Limitation of the dihydroxycinnamic acid series

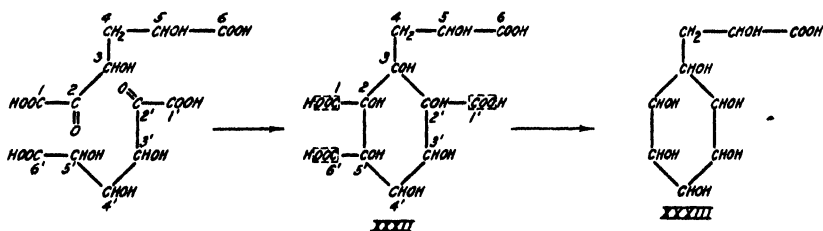


FIG. 27. Derivation of the trihydroxycinnamic acid series

#### DERIVATION OF THE TRIHYDROXYCINNAMIC ACID SERIES

Derivatives of this series found in nature are exemplified by the following:

- 2,4,6 derivatives: limettin, bergaptene
- 3,4,5 derivatives: tricetin, myricetin
- 2,4,5 derivative: aesculetin
- 2,3,4 derivatives: daphnetin, xanthotoxin

The necessary configuration is given by one molecule of a ketosaccharonic acid (derivable from fructose or as under the dihydroxycinnamic series) and one molecule of a ketodicarboxylic acid (derivable from fructose or as under the dihydroxycinnamic series) (figure 27). All trihydroxy derivatives are theoretically possible from XXXIII, but only the 2,4,6-, the 3,4,5-, the 2,4,5-, and the 2,3,4-trihydroxy derivatives have been found in nature.

It is striking that among the naturally occurring products, position 4 always carries a hydroxyl group. This may again be due to the bearing

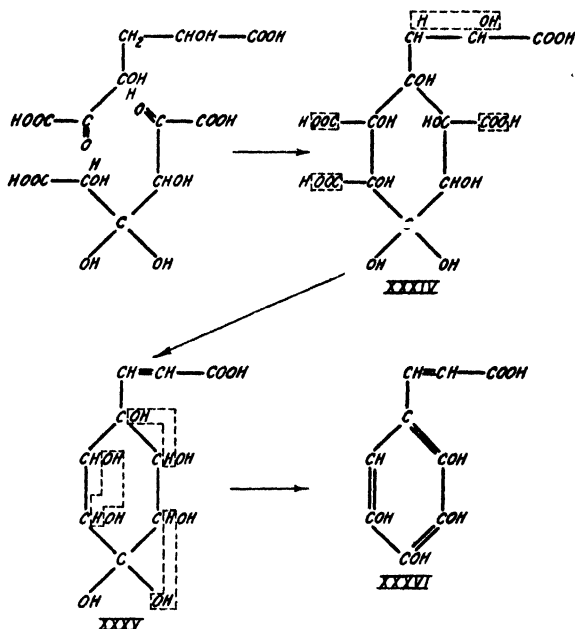


FIG. 28. Derivation of the tetrahydroxycinnamic acid series

of a glycosidally linked radical, which is later removed, on carbon atom 4' in XXXII.

The important gallic acid is conceived of as related to XXXII in the same way that benzoic acid is related to VI. It is also clear that inosite may be related to XXXIII by assuming the oxidation of the side chain to  $\text{—COOH}$ , and subsequent decarboxylation. Quercite may be related similarly to XXVI.

#### DERIVATION OF THE TETRAHYDROXYCINNAMIC ACID SERIES

Such compounds are rare, but apiol and fraxetin are representatives. They may be derived from one molecule of ketose and a second molecule of an oxidized ketose (figure 28).



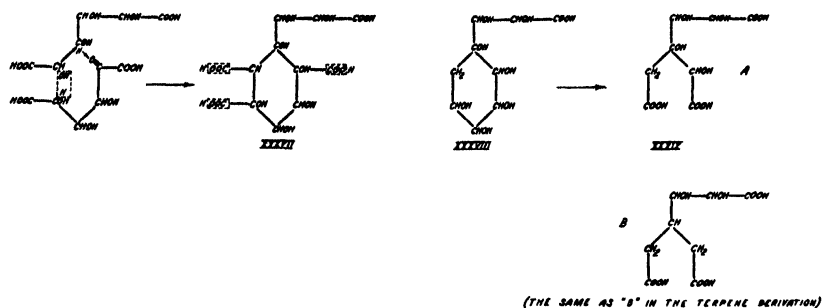


FIG. 29. Half-molecules of carvacrol and thymol

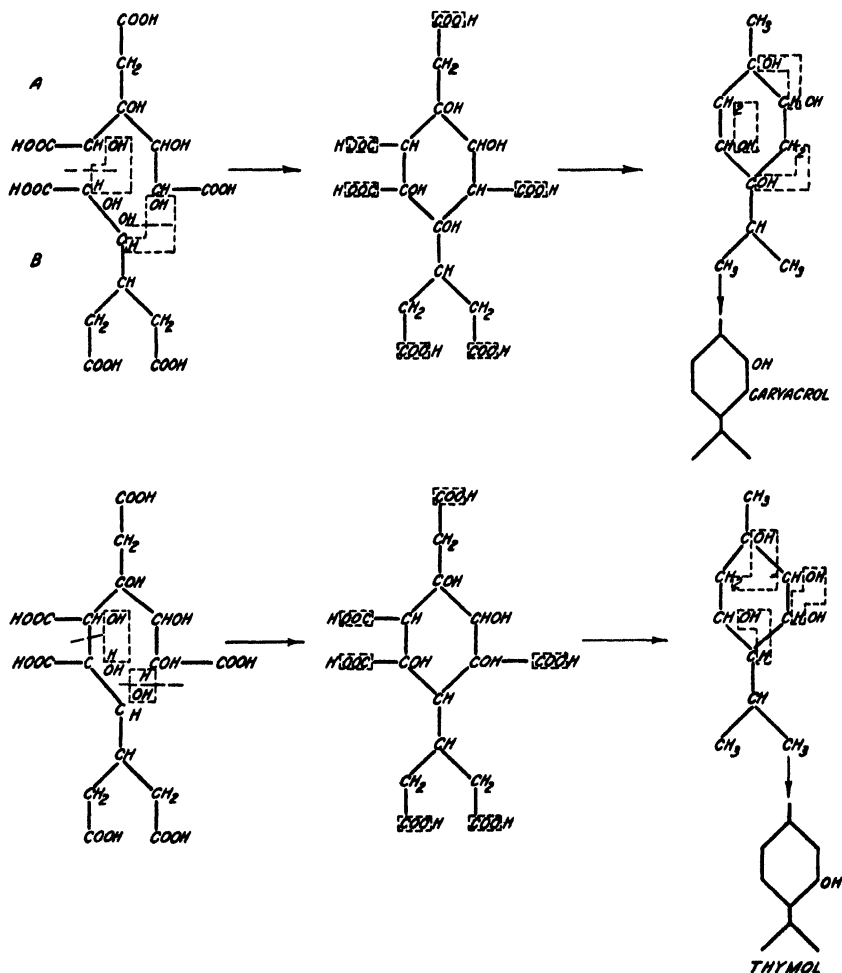


FIG. 30. Derivation of carvacrol and thymol

### DERIVATION OF CARVACROL AND THYMOL

The derivation of carvacrol and thymol is similar to that of the terpenes, but one half of the molecule must be in a higher state of oxidation. Therefore, another half-molecule must be derived, using one molecule of ketose and one molecule of aldose (figure 29), and this must be combined with B of the terpene derivation as in figure 30.

Menthol is derivable in similar manner from B of the terpene derivation and another half-molecule A which must be derived. A is derived from a molecule of the saccharonic type as used before, and a molecule of the saccharonic type in which the  $\text{—CH}_2$  group is in either the 5- or the 2-position (figure 31).

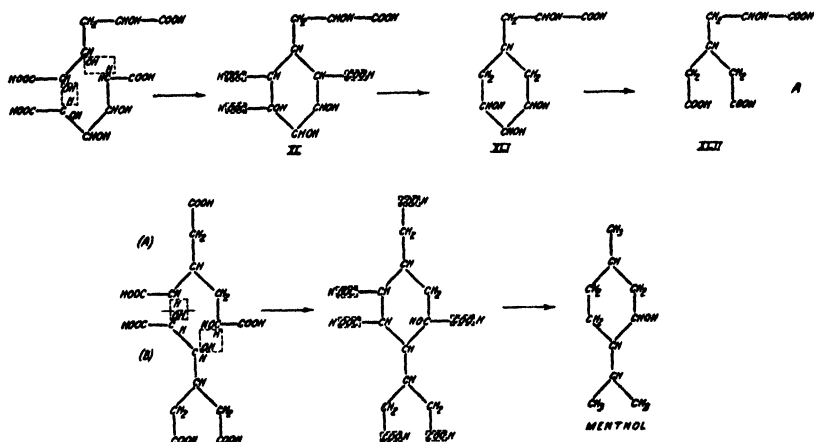


FIG. 31. Derivation of menthol

## METHYLATION

The origin of methoxyl groups and the position of such groups remains to be harmonized with the scheme outlined above. It is clear that positions 3 or 4 in the ring may correspond to position 4 in the hexose chain. A methyl group in either of these positions may represent the residue of an attached chain according to the conception of Browne and Phillips (5). Both position 3 and position 4 in the ring were available for glycosidal linkage in the original hexose molecule. Position 2 in the ring is not found methylated in the mono- and the di-hydroxy series. It first appears in the trihydroxy series in methylated form. It may be more than a coincidence that, in the derivation of this series, two molecules of a fructose derivative are used and that carbon atom 2 of the fructose chain is carbon atom 2 of the ring. Although the corresponding situation exists in the derivation of the dihydroxy group, it is seen that here reversed orientation of the fruc-

tose molecule makes carbon atom 2 of fructose become 3 or 5 in the ring. In the derivation of the trihydroxy group, on the contrary, the two fructose chains must be oriented so that carbon atoms 2 of the chains fall in positions

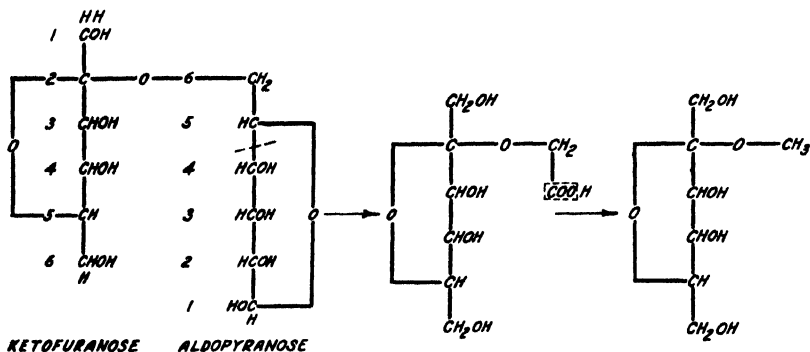


FIG. 32. Development of methoxyl group

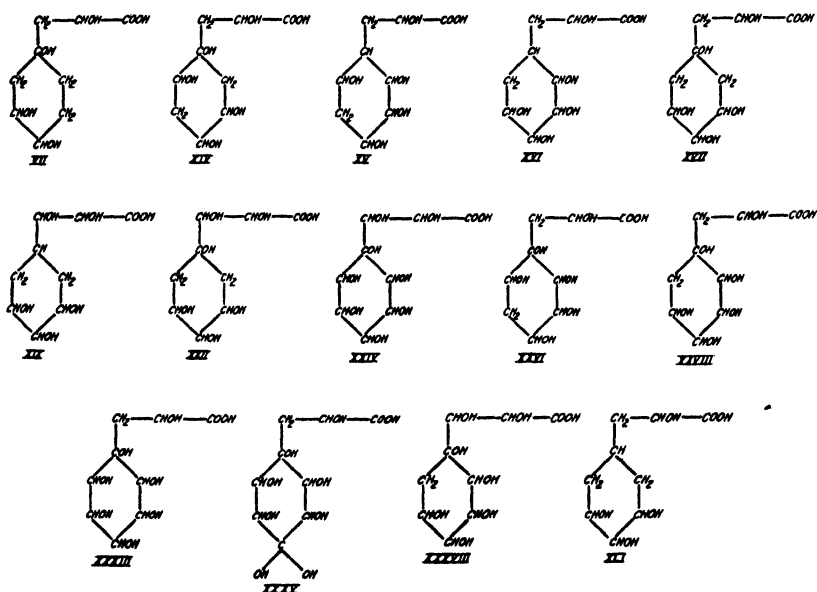


FIG. 33. Decarboxylated intermediates utilized in the foregoing formulations

2 and 6 in the ring. In the ring, positions 2, 3, 4, and 5 are the only ones that occur methylated. Positions 2 and 6 are never occupied simultaneously by methoxyl groups.

The scheme in figure 32 showing the possible development of methoxyl is

TABLE 1

*Acids derivable by simple oxidation from the compounds indicated in figure 33*

ACID	DERIVABLE FROM
Propionic acid, $\text{CH}_3\text{CH}_2\text{COOH}$ . . . . .	VII, XVI, XIX, XLI by way of $\text{CH}_2\text{COOH}$ or $\text{CH}(\text{COOH})_2$ or <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;"> <math>\text{CH}_2\text{COOH}</math>  <math>\text{CH}_2\text{COOH}</math>  <math>\text{CH}(\text{COOH})_2</math> </div> <div style="text-align: center;"> <math>\text{CH}(\text{COOH})_2</math> </div> </div>
Butyric acid, $\text{C}_4\text{H}_7\text{COOH}$ . . . . .	XVI, XIX, XLI
Isobutyric acid, $(\text{CH}_3)_2\text{CHCOOH}$ . . . . .	XVI, XIX, XLI
<i>n</i> -Valeric acid, $\text{C}_5\text{H}_9\text{COOH}$ . . . . .	Not possible
Isovaleric acid, $(\text{CH}_3)_2\text{CHCH}_2\text{COOH}$ . . . . .	XLI
Methacrylic acid, $\text{CH}_2=\text{C}(\text{CH}_3)\text{COOH}$ . . . . .	VII, XVII, XIX, XXII, XXVIII
Angelie and tiglic acids, $\text{CH}_3\text{CCOOH}$ . . . . .	VII, XV
<div style="text-align: center;"> <math>\text{CH}_3\text{CH}</math>  <math>\parallel</math> </div> $\beta, \beta$ -Dimethylacrylic acid, $(\text{CH}_3)_2\text{C}=\text{CHCOOH}$ . . . . .	VII, XVII, XIX, XXII
Malonic acid, $\text{CH}_2(\text{COOH})_2$ . . . . .	VII, XIV, XV, XVI, XVII, XIX, XXII, XXVI, XXVIII, XXXIII, XXXV, XXXVIII, XLI
Succinic acid, $\text{C}_2\text{H}_4(\text{COOH})_2$ . . . . .	VII, XV, XVI, XIX, XLI
Glutaric acid, $(\text{CH}_2)_3(\text{COOH})_2$ . . . . .	XVI, XIX, XLI
Fumaric acid, $\text{HOOCCH}=\text{CHCOOH}$ . . . . .	VII, XIV, XV, XVI, XVII, XIX, XXII, XXVI, XXVIII, XXXIII, XXXV, XXXVIII, XLI
Maleic acid, $\text{CHCOOH}=\text{CHCOOH}$ . . . . .	VII, XIV, XV, XVI, XVII, XIX, XXII, XXVI, XXVIII, XXXIII, XXXV, XXXVIII, XLI
Mesaconic acid, $\text{CH}_3\text{CCOOH}$ . . . . .	VII, XIV, XV, XVII, XIX, XXII
Tricarballic acid, $\text{CH}_2\text{COOH}=\text{CHCOOH}=\text{CHCOOH}$ . . . . .	XVI, XIX, XLI
Aconitic acid, $\text{CH}_3\text{COOH}=\text{CHCOOH}=\text{CHCOOH}$ . . . . .	VII, XIV, XV, XVII, XXII, XXVIII

TABLE 1—*Concluded*

ACID	DERIVABLE FROM
$\alpha, \beta$ -Dihydroxy- $\alpha$ -methylbutyric acid, $\text{CH}_3\text{CHOHC}(\text{OH})\text{COOH} \dots \dots \dots$	XIV, XXVI
$\begin{array}{c} \text{CH}_3 \\   \\ \text{Malic acid, } \text{CH}_2\text{COOH} \dots \dots \end{array}$	VII, XIV, XVII, XXII, XXVIII
$\begin{array}{c} \text{CHOH} \\   \\ \text{CH}_2\text{COOH} \\ \text{Tartaric acid, } \text{CHOHCOOH} \dots \dots \end{array}$	VII, XIV, XV, XVI, XVII, XIX, XXII, XXVI, XXVIII, XXXIII, XXXV, XXXVIII, XLI
$\begin{array}{c} \text{CHOHCOOH} \\   \\ \text{Citric acid, } \text{CH}_2\text{COOH} \dots \dots \end{array}$	VII, XIV, XVII, XXII, XXVIII
$\begin{array}{c} \text{C}(\text{OH})\text{COOH} \\   \\ \text{CH}_2\text{COOH} \\ \text{Isocitric acid, } \text{CH}_2\text{COOH} \dots \dots \end{array}$	XV, XVI
$\begin{array}{c} \text{CHCOOH} \\   \\ \text{CH}(\text{OH})\text{COOH} \end{array}$	

supplementary to those shown by Browne and Phillips (5). Other similar possibilities at once suggest themselves.

The decarboxylated intermediates utilized in the foregoing formulations are assembled in figure 33. Systematic combination of these structures, as indicated in figure 15, extends the possibilities over a very large field.

The acids shown in table 1 may be derived from them by simple oxidation.

#### NITROGENOUS SUBSTANCES

A generalized scheme of phytosynthesis should be applicable to the naturally occurring nitrogenous compounds, and especially to the amino acids upon which seems to rest the whole structure of protein and alkaloid synthesis (39).

As pointed out by Stewart (50) the initial steps by which nitrogen as nitrate from the soil is made to appear in combination with carbon, hydrogen, oxygen, and sometimes sulfur and phosphorus, are still obscure. However, considerable evidence is found of the existence in the plant of a hexose-nitrogen compound in which an amino group occurs on the second carbon

atom of the hexose chain. Diehl (9) affirms the identity of vegetable chitin with animal chitin and Van Iterson (29) has confirmed the same thing by means of x-ray diagrams.

Vestigial evidence is found in the formula for lactoflavin of Kuhn (34), and in the accepted formulas for inosic acid and adenosin (figure 34).

In nearly all the known amino acids, if the carboxyl group be assumed to represent carbon atom 1 of an original hexose chain, a nitrogen atom is

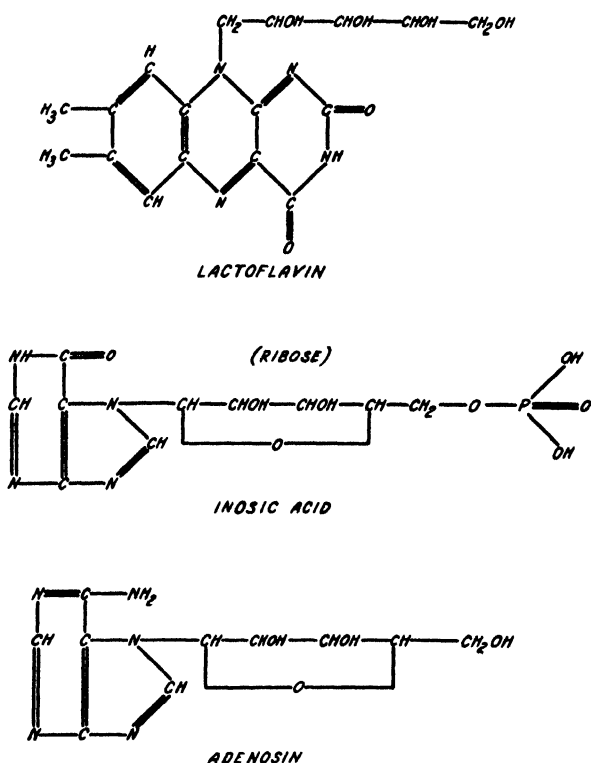


FIG. 34. Evidence for existence of a hexose-nitrogen compound

found attached to carbon atom 2. Furthermore, an examination of the formulas of the amino acids shows a very marked recurrence of the three-carbon atom chain that is so prevalent among non-nitrogenous bodies. It is distinct in the members of the series shown in figure 35. In the remaining members the chain is present, although not in such pronounced form. It is at once suggested that the application of the methods used in the non-nitrogenous derivations to condensations involving a 2-amino-hexose chain should be instructive.



follow naturally, as in the similar derivations of the hydroxycinnamic acid series.

If now, the various decarboxylated products that were utilized in the derivations of the non-nitrogenous compounds be written in  $\alpha$ -amino acid form, the series of intermediates shown in figure 37 becomes possible. In this series the numbering is the same as before, with the prefix "N."

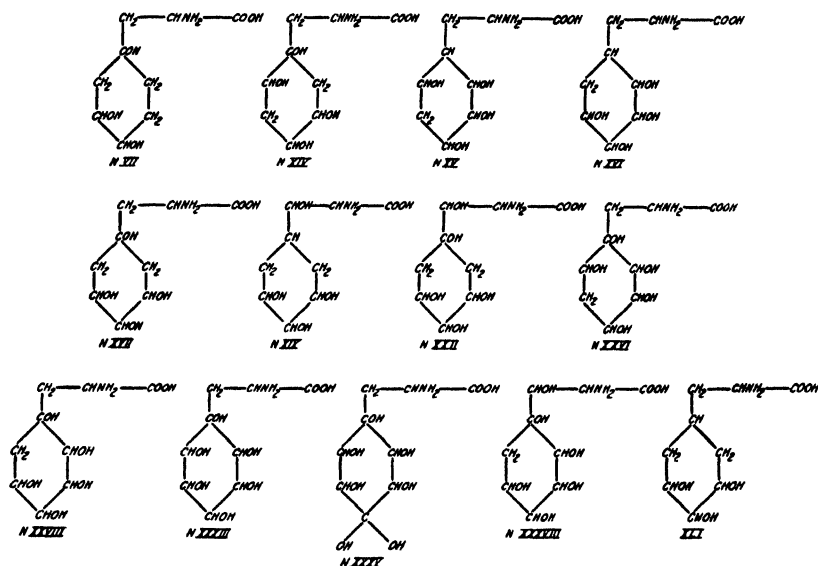


FIG. 37. Decarboxylated intermediates written in  $\alpha$ -amino acid form

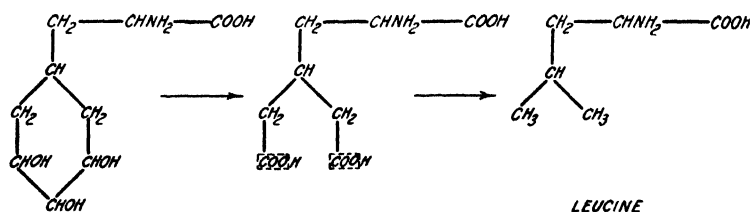


FIG. 38. Derivation of leucine

Oxidation of the cycle, in a manner analogous to the derivation of the terpene "half-molecules," gives several amino acid derivations directly. Thus oxidation of N XII gives leucine, as shown in figure 38. Norvaline may be conceived as derived from N XVI;  $\alpha$ -aminobutyric acid from N XV; aspartic acid from N XXVI, N XXXIII, or N XXXV; glutamic acid from N XV; and oxyglutamic acid perhaps from N XIX. Proline seems to require as a precursor a cyclization between a hydroxyl group and the



amino group. This might follow as indicated in figure 39. A similar derivation of oxyproline from N XXXIII is at once suggested.

Condensation of two molecules of  $\alpha$ -amino-hexose derivatives in the same manner as before should lead to some of the diamino acids. A derivation of ornithine is shown in figure 40. Elimination of ammonia and the use

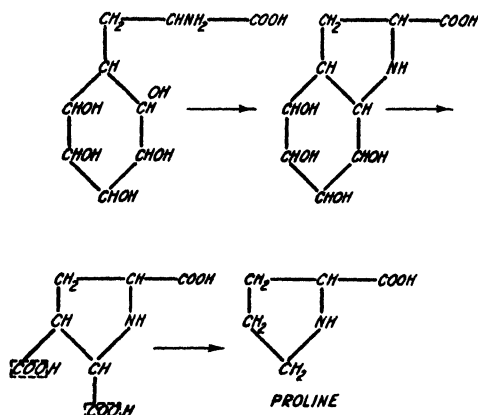


FIG. 39. Derivation of proline

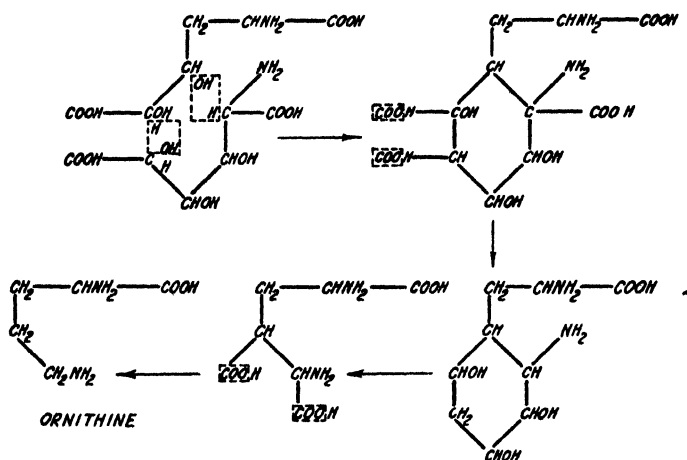


FIG. 40. Derivation of ornithine

of other hydroxylated configurations makes possible a large series of pyrrolidine and pyrrole derivatives. A reversal of the orientation as in the condensation in figure 40 may lead to lysine, as in figure 41. In histidine, arginine, and tryptophane, the same chain,  $\text{—CH}_2\text{—CHNH}_2\text{—COOH}$ , is present as in the other amino acids, but the derivation of the other parts of the molecules is more obscure.

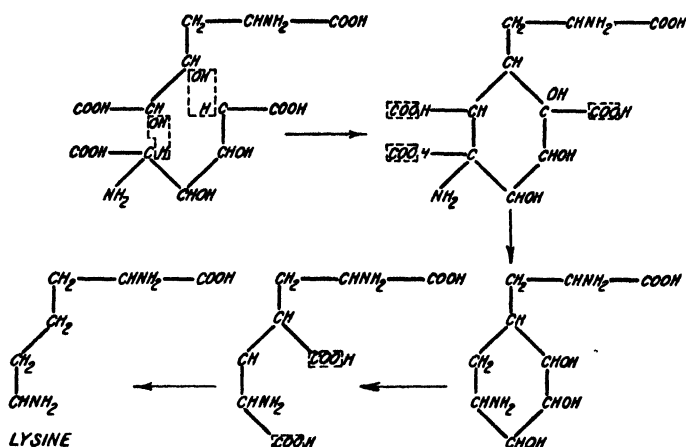


FIG. 41. Derivation of lysine

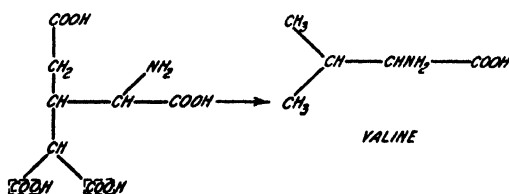


FIG. 42. Derivation of valine

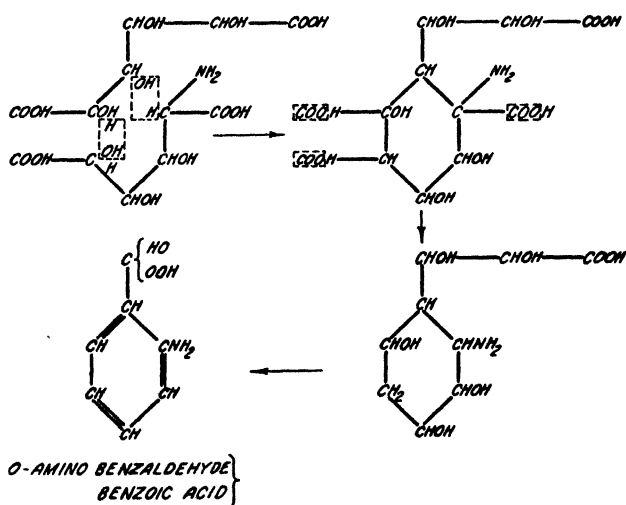


FIG. 43. Derivation of o-aminobenzaldehyde or o-aminobenzoic acid

Glycine, alanine, serine, and cysteine seem to offer no special difficulties, once the underlying 2-amino sugar is assumed to exist. Valine seems to be a special case in which some such configuration as shown in figure 42 is required to fit it into the scheme. The derivation of *o*-aminobenzaldehyde or *o*-aminobenzoic acid seems rather important as the starting point for a large number of compounds. A possible derivation is shown in figure 43. The type of condensation shown in this figure, amplified by using the various modifications already employed in other connections, gives a further wide range of possible derivatives.

Only a beginning has been made here in the derivation of the nitrogenous substances, and those related compounds containing sulfur have not been treated. Completeness has not been the aim; rather, an attempt has been made to lay a foundation in harmony with the derivation of the non-nitrogenous groups.

#### CONCLUSION

The intricate problems of phytosynthesis cannot be solved by mere structural formulations but the latter, properly interpreted, can suggest lines of laboratory approach that have been almost entirely lacking. The foregoing formalized presentation of a coördinated and unified method of regarding some of the phases of phytosynthesis strongly suggests that such lines of laboratory approach must be radically different from those of conventional organic methods.

There is no experimental testimony in support of the type of union between hexose chains that is postulated as the principal reaction involved in the development of all the phytosyntheses that have been worked out in this paper. Yet the comparative simplicity and uniformity in character of the subsequent derivations, the relating in synthesis of classes of compounds that are related physiologically, and, above all, the apparently very broad possible application of the methods involved give weight to the belief that fundamental relationships are being approached. The underlying suppositions can be said then to constitute a sort of pragmatism which may approach the rank of a theory if and when they receive the support of laboratory evidence. If, in the meantime, they may aid in unifying thought in the field of phytosynthesis and stimulating a new type of laboratory approach, they will have served a sufficient purpose.

The author wishes to acknowledge with deep gratitude the helpful criticism and stimulating advice of Professor Edward Kremers, whose many former students will readily recognize and properly place the source of inspiration for the type of reasoning employed in this contribution.

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# THE REACTIONS OF PURE HYDROCARBONS IN THE PRESENCE OF ALUMINUM CHLORIDE<sup>1</sup>

GUSTAV EGLOFF, EDITH WILSON, GEORGE HULLA, AND  
P. M. VAN ARSDELL

*Universal Oil Products Company, Chicago, Illinois*

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## I. INTRODUCTION

Reactions of pure hydrocarbons of the paraffin, olefin, acetylene, cycloparaffin, cycloolefin, terpene, and aromatic series which occur in the presence of aluminum chloride are finding application for the production of isomers and lower and higher hydrocarbons. Many studies have been made, and it is believed that more information as to the reactions and mechanisms could be developed by a digest of all the recorded work. In the seven groups of hydrocarbons studied in the presence of aluminum chloride, the reactions of dissociation, dehydrogenation, hydrogenation, isomerization, cyclization, polymerization, alkylation, and aromatization play principal rôles, with some exceptions. A striking fact stands out, namely, that the butanes, particularly isobutane, are key hydrocarbons resulting from many of these reactions.

Owing to a lack of definite knowledge of the exact rôle of aluminum chloride in hydrocarbon reactions, in the broadest sense it is looked upon as a catalyst. From the standpoint of the mechanism of the reaction, it becomes of interest to know if the aluminum chloride functions as a catalyst, as a component part of the reaction, or as both. The changes taking place with pure hydrocarbons, with some exceptions, in the presence of aluminum chloride seem to be a variation of the Friedel-Crafts reaction. In some cases, aluminum chloride reacts with the hydrocarbon to give hydrogen chloride (44, 100), which in turn reacts with another hydrocarbon molecule. In other cases, a complex compound containing hydrogen chloride, aluminum chloride, and hydrocarbon is produced. There are a number of hydrocarbons which do not react readily in the presence of aluminum chloride, but do when hydrogen chloride is added. The formation of alkyl chlorides has not been shown in all reactions,

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which is explained by the fact that at certain temperatures alkyl chlorides are unstable compounds in the presence of aluminum chloride and form olefins or other reaction products; however, in the case of the methylated benzenes, methyl chloride results under vigorous experimental conditions.

All forms of aluminum chloride are not adapted to use as a catalyst, as the method of preparation has an effect on the nature of its action. It was found (21) that with aluminum chloride prepared from hydrogen chloride and aluminum, the reaction of benzene and acetylene proceeded slowly, but with that prepared from aluminum and chlorine the action was rapid. Freshly prepared aluminum chloride (27) was found to be too active for the same reaction, and any degree of activity could be obtained by aging for various periods of time. More liquid products were formed when freshly prepared aluminum chloride was used in the polymerization of ethylene (86), and its activity may be due to the physical state rather than to the agents used in preparation and the time elapsing before use.

The reactions of pure hydrocarbons in the presence of aluminum chloride are usually characterized by the formation of colored reaction mixtures. The color usually appears when aluminum chloride comes in contact with the hydrocarbon. This would seem to indicate that the color was caused by some change in the nature of the aluminum atom. Color is a characteristic property of certain complex compounds, and since aluminum chloride forms complexes with hydrocarbons, there is a probable relationship. The cause of these colors is unknown, and they cannot be considered necessary for the occurrence of a reaction since colorless reaction mixtures are known.

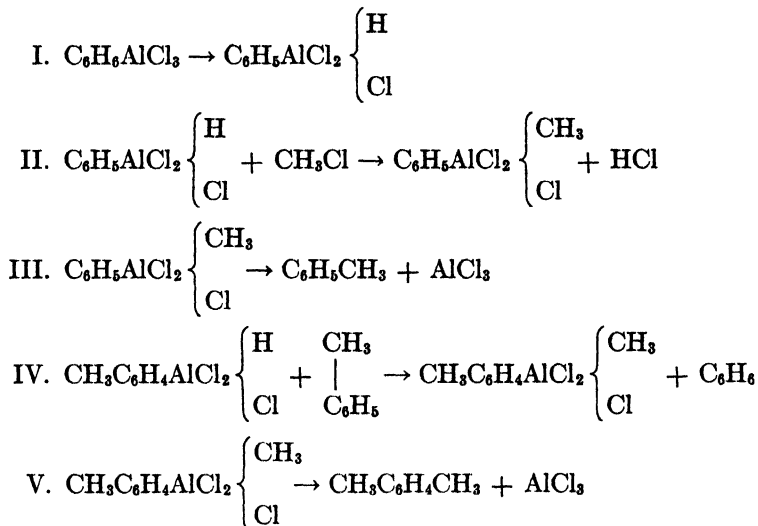
Hydrocarbon reactions are not induced by aluminum chloride hexahydrate. Its water of crystallization is held strongly enough to shield the forces of attraction in the aluminum chloride hydrate molecule, thereby preventing formation of complexes with hydrocarbons.

Numerous addition compounds of hydrocarbons are formed with aluminum chloride, as shown in table 18. Two types (60, 61, 62, 63) of complexes are recognized: (1) addition compounds of aluminum chloride with unit amounts of an aromatic or unsaturated hydrocarbon; (2) addition compounds with greater than unit amounts of hydrocarbon. The complexes of the first type are very reactive (60) towards ether, acetone, and aromatic hydrocarbons. With the aromatic hydrocarbons, complexes of the second type are formed, having high dissociation pressures. Hence, the first-type complexes are considered as "hydrocarbon of constitution," analogous to water of constitution. It is of interest to recall that  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$  upon heating retains one molecule of water of crystallization with greater strength than the other four. The simpler aluminum chloride hydrocarbon complexes act similarly.

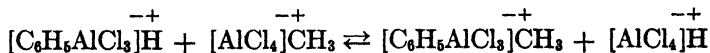
In many of these reactions hydrogen chloride is a highly important

component of the system; it may be added to the reaction, or may be present as a result of hydrolysis of the aluminum chloride by water, or may arise as a product of the hydrocarbon reaction.

Aluminum chloride has been thought of as a hydrohalogenating-dehydrohalogenating agent. This involves the formation and decomposition of complex compounds in which hydrogen chloride acts as part of the reaction system. The series of reactions (126) for benzene, toluene, and aluminum chloride which will serve as an example are shown as follows:



An ionic equilibrium as the mechanism of reaction, whereby active hydrogen and methyl ions are interchangeable, is given (112):



Conductance measurements (149) show that there is but little ionization in a benzene solution of aluminum bromide. A small amount of ethyl bromide slightly increases the conductance of a solution of aluminum bromide in benzene, and a small amount of benzene increases the conductance of aluminum bromide in ethyl bromide, whereupon reaction follows. Evidence was obtained for the formation of an aluminum bromide and hexaethylbenzene complex, to which is ascribed the formula,



The corresponding crystalline substance,  $2\text{AlBr}_3 \cdot \text{C}_6(\text{C}_2\text{H}_5)_6$ , was also obtained (83).

The rôle of polarity and energy change in aluminum chloride reactions is shown (112) as:



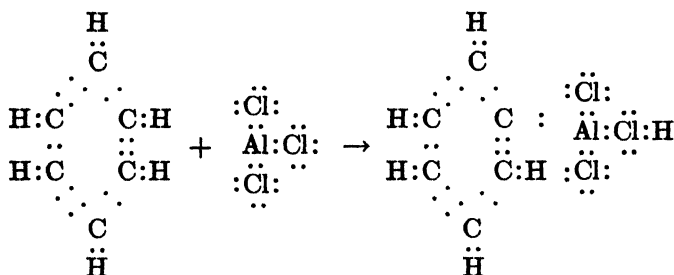
Non-polar molecule  $\rightarrow$  polar molecule  $- Q_1$

Polar molecule + catalyst  $\rightarrow$  addition product +  $Q_2$

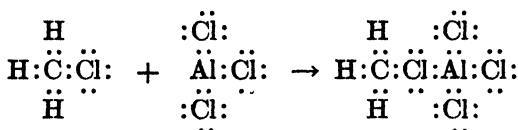
Non-polar molecule + catalyst  $\rightarrow$  addition product +  $Q_2 - Q_1$

The octet theory of valence offers another viewpoint in these mechanisms. The aluminum atom of the chloride requires two electrons to complete its shell (36), and therefore unites readily with the chloride of an alkyl chloride, which is able to share two of its electrons with aluminum.

The aluminum chloride reaction can be interpreted in the light of the octet theory. Addition compounds are formed according to two equations:



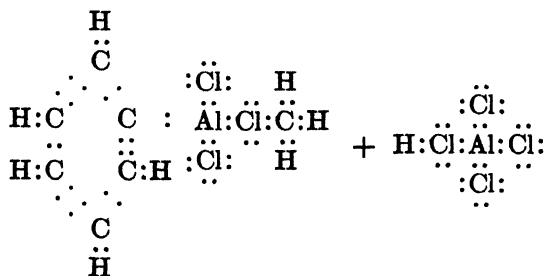
Benzene

A  
Phenyl-hydrogen-  
aluminum chloride

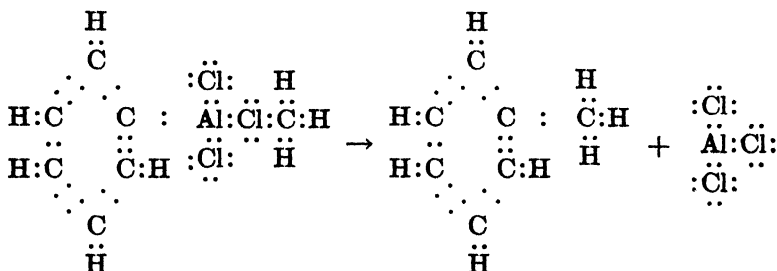
Methyl chloride

B  
Chloro-methyl-  
aluminum chloride

Then double decomposition occurs between the complexes A and B to form:

Phenyl-methyl-  
aluminum chlorideChloro-hydrogen-  
aluminum chloride

The compound  $[C_6H_5AlCl_3]^{+}CH_3$  is identical with  $C_6H_5AlCl_2 \begin{Bmatrix} CH_3 \\ Cl \end{Bmatrix}$ , and further decomposition is represented by the following equation:

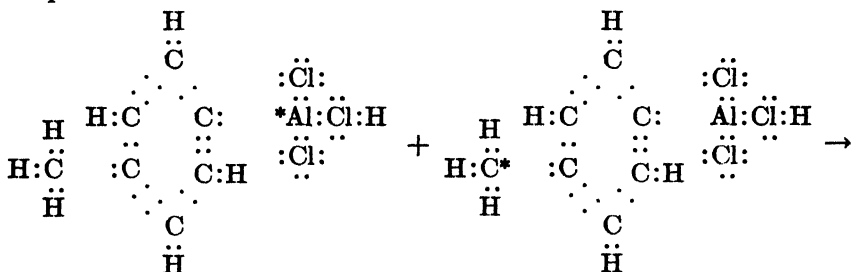


Phenyl-methyl-aluminum chloride      Toluene

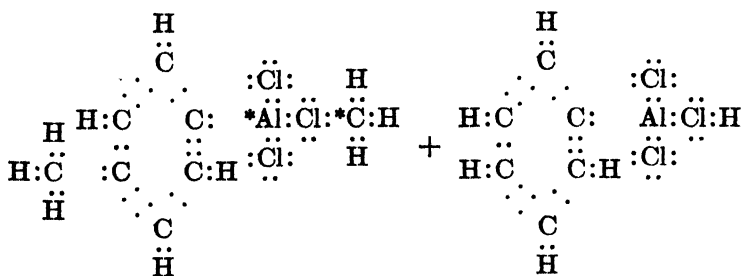
The action of aluminum chloride on toluene (126) with the formation of benzene and xylenes may be reinterpreted by the octet theory. First, a toluene-aluminum chloride complex is formed, corresponding to



Then, double decomposition occurs between electromeric forms of the complex so formed:

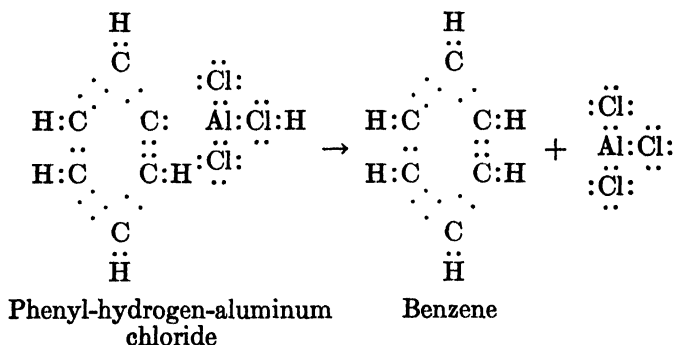
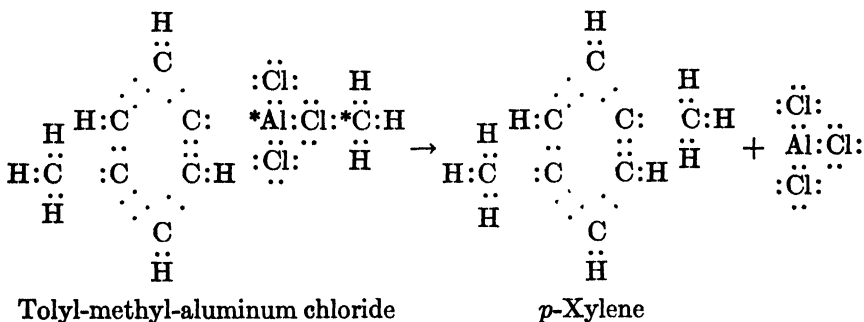


Tolyl-hydrogen-aluminum chloride      Tolyl-hydrogen-aluminum chloride



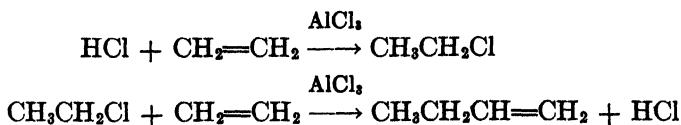
Tolyl-methyl-aluminum chloride      Phenyl-hydrogen-aluminum chloride

Asterisks have been introduced in these equations corresponding to a shift of the electron doublet which makes the methyl group positive relative (90) to the aromatic nucleus. The final decompositions are shown in the equations:



The sharing of electrons will be affected by the difference in bond strength in the various hydrocarbons. At present, it is impossible to say just where all hydrocarbons share electrons with the aluminum atom.

Ethylene is reported to react in the presence of aluminum chloride only when hydrogen chloride is present. The addition of hydrogen chloride to the ethylene molecule under the influence of aluminum chloride is thought to be the primary step in the mechanism (77), which is followed by a coupling of the ethyl chloride with another ethylene molecule and the separation of hydrogen chloride.



Propene acts similarly in the presence of floridin, and it is probable that the formation of an alkyl chloride may be a general reaction for olefins and

hydrogen chloride. This mechanism does not necessarily involve the formation of complexes of aluminum chloride with olefins, although it is known that these do form. In the alkylation of benzene by ethylene in the presence of aluminum chloride, hydrogen chloride is necessary (16).

Hydrogen bromide is exceptionally effective (51) in activating aluminum chloride, and that activation is possible prior to hydrocarbon introduction. This indicates that the catalyst in its active form is a hydrogen-halide-aluminum chloride, which gives support to the octet interpretation but does not necessarily conflict with an alkyl halide mechanism.

The above theories stress the effect of aluminum chloride and hydrogen chloride, but they do not consider the difference due to the hydrocarbon structure. Reactions are induced by fundamental differences in structure (90, 131); therefore, the aluminum chloride reaction analogously must involve primary, secondary, tertiary, and quaternary carbon atoms and the structure of the hydrocarbon groups attached thereto, and also their initial activity and final stability. Complexes with olefins, acetylene, and aromatics are known. Although no complex compounds of aluminum chloride and paraffins have been reported as yet, it is an excellent catalyst in most paraffin reactions. In particular, the activity of the tertiary hydrocarbon group and, to a lesser extent, that of the secondary is greatly enhanced by the presence of aluminum chloride and hydrogen chloride (53).

Although reactions between either aluminum chloride or hydrogen chloride and the hydrocarbon do occur, these intermediate reactions have not been shown to be a necessary factor for the formation of the end products. Formation of hydrogen chloride or methyl chloride may be a secondary reaction where part of the aluminum chloride acts in a metathetical way. The effect of aluminum chloride on the weakening of the bonds in the hydrocarbon leads one to expect a difference in the nature of the products, depending on the concentration of the aluminum chloride. The products produced will also depend on factors such as temperature, pressure, the presence of a solvent (137), or water.

The activity of aluminum chloride with hydrocarbons may be modified by organic liquids (39), such as acetone, acetophenone, nitrobenzene, and nitromethane. The shielding effect of water of crystallization in aluminum chloride hexahydrate suggests that these liquids, owing to their high dielectric properties and solubility, act to shield the effective centers of anhydrous aluminum chloride by reducing the fields of force. Such compounds (106) are associated liquids possessing high dielectric properties which favor ionization. Furthermore, aluminum chloride in solution has dielectric properties consistent with an increase in activity of dissolved hydrocarbons. Paraffins show an absence (25, 128) of dipole moment or polarity in their molecules, but there must still be sufficient differences in the

TABLE 1  
*Reactions of paraffins*

COMPOUNDS	TEMPERATURE	TIME	CONCENTRATION OF $\text{AlCl}_3$	PRESSURE	PRODUCTS		REMARKS
					Gases	Liquids and solids	
$\text{CH}_4$ .....	°C. 200 370-500	hours 8-120 40	per cent	atmospheres Sealed tube	Above 370°C. $\text{H}_2$ formed; $\text{HCl}$ (due to presence of $\text{H}_2\text{O}$ )	At 500°C. carbon formed; no liquid formed	(89)
$\text{C}_2\text{H}_6$ .....	320-500	72-40		Sealed tube	Above 370°C. $\text{H}_2$ formed; $\text{HCl}$	At 410°C. carbon formed and an oil	(89)
$\text{C}_3\text{H}_8$ .....	300-500	40		Sealed tube	Above 320°C. $\text{H}_2$ formed; $\text{HCl}$	At 320°C. oil formed; carbon at 420°C.	(89)
$\text{C}_4\text{H}_{10}$ .....	200	10	33 3	70	Ethane, 5 per cent; methane, 2 per cent	Heavy oil	(79)
$n\text{-C}_4\text{H}_{10}$ .....	345-500	40-24		Sealed tube	Above 245°C. $\text{H}_2$ formed	At 350°C. liquid formed	(89)
$\text{iso-C}_4\text{H}_{10}$ .....	245-500	200-40		Sealed tube	Isobutane, 17 per cent; propane, 54 per cent; ethane, 10 per cent; methane, 5.8 per cent; hydrogen, 0.1 per cent	At 245°C. liquid formed	(89)
$n\text{-C}_4\text{H}_{10} + \text{HCl}$ ...	175	3-4	31	35	Butanes; isopentane; hydrogen, trace	Heavy brown oil	(78)
$n\text{-C}_5\text{H}_{12}$ ..	36	5-10 days	23-28 <sup>(1)</sup>	1	Butanes; isopentane	Tar	(51)
$n\text{-C}_5\text{H}_{12} + \text{nitrogen}$ .	40-133		100 (at start)	1	Butanes; isopentane; hydrogen, trace	Liquids, 85-90 per cent; tar	(51)
$\text{C}_6\text{H}_{14}$ <sup>(d)</sup> ..	20-110	72-10	37-73 <sup>(a)</sup>	Sealed tube	Saturated hydrocarbons	$\text{C}_4\text{H}_8$ , $\text{AlBr}_3$	(57)
$\text{C}_6\text{H}_{14}$ .....	100		83-40 <sup>(b)</sup>	1	Butane (large); propane	Pentane; higher hydrocarbons	(48)
$\text{C}_6\text{H}_{14}$ .....	15-55	350				No reaction except when catalyzed by $\text{C}_2\text{H}_5\text{Br}$	(120)

$C_4H_{10}$ .....	100	7½	27	1	No gases	2- or 3-methylpentane; cyclohexane	(104)
$C_4H_{10} + HCl$ .....	69-72	3	9	35	Isobutane, 90 per cent; pentane, 9 per cent; hexane, 1 per cent	Isomeric hexanes; saturated hydrocarbons (b.p. $-10^\circ$ to $200^\circ C$ .); unsaturated hydrocarbons	(78)
$n-C_4H_{10}$ .....	80	1.5	5	Sealed tube		Isomeric hexanes, 2 per cent	(100)
$n-C_4H_{10}$ .....	90	1	5	Sealed tube		Isomeric hexanes, 4 per cent	(100)
$n-C_4H_{10}$ .....	90	2	4	Sealed tube		Isomeric hexanes, 20 per cent	(100)
$n-C_4H_{10}$ .....	90	3	4	Sealed tube		Isomeric hexanes, 23 per cent	(100)
$n-C_4H_{10}$ .....	90	1	5(e)	Sealed tube		Isomeric hexanes, 25 per cent	(100)
$n-C_4H_{10}$ .....	90	2	5(e)	Sealed tube		Isomeric hexanes, 28 per cent	(100)
$n-C_4H_{10}$ .....	45	1	5(e)	Sealed tube		Isomeric hexanes, 23 per cent	(100)
$n-C_4H_{10}$ .....	45	3	5(e)	Sealed tube		Isomeric hexanes, 25 per cent	(100)
$C_7H_{16}$ .....	100	10	25	1	Propane; isobutane (small amounts)		(104)
$C_7H_{16}$ .....	100	10	30(e)	1	Propane; isobutane (larger amount than with the anhydrous)	2- or 3-methylpentane; heptane; 1,3-dimethylcyclohexane; methylcyclohexane; cyclohexane; bicyclic paraffins	(104)
$C_7H_{16}$ .....	220	3	1	50		Isomers, 8 per cent	(111)
$C_7H_{16}$ .....	100			1		2-Methylhexane; hexane	(24)

(i) 0.6 to 0.8 per cent of water added.

(e) 3 per cent of 1-chloropropane added.

(f) 4 per cent of 1-chloropropane added.

(g) 10 per cent of  $PbSO_4 \cdot 2HCl$  added.(h) 10 per cent of  $CuSO_4 \cdot 2HCl$  added.(a)  $AlBr_3$ .

(b) Added in four parts.

(c) 1 per cent of water added.

(d)  $C_2H_5Br$  added.

TABLE 1—Concluded

COMPOUNDS	TEMPERATURE	TIME	CONCENTRATION OF $\text{AlCl}_3$	PRESSURE	PRODUCTS		REFERENCES
					Gases	Liquids and solids	
$\text{C}_7\text{H}_{16}$ .....	$^{\circ}\text{C}$ . 96	hours	per cent 63.1	atmospheres 1		Basis: 100 parts of <i>n</i> -heptane reacted— Pentanes and below 64.6 2-Methylpentane 3.4 3-Methylpentane 2.0 <i>n</i> -Hexane 0.4 2,4-Dimethylpentane 1.5 2,2,3-Trimethylbutane 0.5 3,3-Dimethylpentane 0.4 2-Methylhexane 1.2 3-Methylhexane 1.6 Polymerization products 24.4	(23)
$\text{C}_7\text{H}_{16} + \text{H}_2\text{O}$ .....	97-99	3	9	35	Propane, 2 per cent; isobutane, 81 per cent; heptane, 13 per cent; butane + hexane, 4 per cent	Paraffins boiling below and above heptane; unsaturated hydrocarbons (small)	(78)
$n\text{-C}_8\text{H}_{18}$ . . . . .	20	1	8 <sup>(1)</sup>	Sealed tube		Isomeric octanes, 13 per cent	(100)
$n\text{-C}_8\text{H}_{18} + \text{HCl}$ . . . . .	20	22	5			Isomeric octanes, 24.0 per cent	(100)
$n\text{-C}_8\text{H}_{18}$ . . . . .	20	22	10 <sup>(a)</sup>			Isomeric octanes, 17.5 per cent	(100)
$n\text{-C}_8\text{H}_{18}$ . . . . .	20	22	10 <sup>(b)</sup>			Isomeric octanes, 24.3 per cent	(100)
$n\text{-C}_8\text{H}_{18} + \text{HCl}$ . . . . .	20	15	10			Isomeric octanes, 5 per cent	(100)
$n\text{-C}_8\text{H}_{18} + \text{HCl}$ . . . . .	20	4	10			Isomeric octanes, 15 per cent	(100)

$n\text{-C}_4\text{H}_{10} + \text{HCl} \dots$	20	6	10				Isomeric octanes, 19 per cent	(100)
$n\text{-C}_4\text{H}_{10} + \text{HCl} \dots$	20	8	10				Isomeric octanes, 24 per cent	(100)
$n\text{-C}_4\text{H}_{10} + \text{HCl} \dots$	20	24	10				Isomeric octanes, 38 per cent	(100)
$n\text{-C}_4\text{H}_{10} + \text{HCl} \dots$	20	96	10				Isomeric octanes, 61 per cent	(100)
$n\text{-C}_4\text{H}_{10} \dots$	115-125	8	23	1		$n\text{-Butane}$	Liquid (b.p. 70-120°C.)	(52)
$\text{C}_4\text{H}_{10} \dots$	405-410	3	5	70			Isomers, 23 per cent	(111)
2,5-Dimethylhexane ...	100-110	6	22	1		HCl; $n\text{-butane}$ ; tetramethylmethane	Unsaturated hydrocarbons	(52)
2,2,4-Trimethylpentane + HCl ...	20-50	4	9	1		Isobutane, 92 per cent; pentane, 8 per cent	Paraffinic hydrocarbons corresponding to heptanes, nonanes, heptadecane; unsaturated oil	(53)
$\text{C}_5\text{H}_{12} \dots$	110-120	8	30	1		$n\text{-Butane}$	Believed amylene→cyclopentane; amylene polymers	(34)
$n\text{-C}_{10}\text{H}_{22} \dots$	140-150	8	26 3	1		$n\text{-Butane}$	Liquid (b.p. 69-73°C.)	(52)
2,7-Dimethyloctane. 135-145		4	37 5	1		$n\text{-Butane}$ ; tetramethylmethane	Cyclopentane; liquid (b.p. 50-170°C.)	(52)
2,7-Dimethyloctane. 135-145		4	28 5	1		Less gas than in the above experiment	Aliphatic hydrocarbons; liquid (b.p. 50-180°C.)	(52)
2,7-Dimethyloctane. 110-120		7	16	1		$n\text{-Butane}$ ; tetramethylmethane	Believed dodecanes; tridecanes; liquid (b.p. 90-285°C.)	(52)
$\text{C}_6\text{H}_{14} \dots$	150-200		33.3	1		$n\text{-Butane}$ (large); propane	Higher hydrocarbons	(50)
$\text{C}_{17}\text{H}_{36} \dots$	150-160	4	14	1		$n\text{-Butane}$	Saturated hydrocarbons	(52)
$\text{C}_{18}\text{H}_{38} \dots$	110		20	1		Paraffins	Liquids, 60 per cent; heavy oil, 3.3 per cent; carbon, 23 per cent	(13)
$\text{C}_8\text{H}_{18} \dots$	150		20	1		Paraffins	Liquids, 33 per cent; heavy oil, 30 per cent; carbon, 24 per cent	(13)



rigidity of hydrocarbon groups and of hydrogen to account for activity in the manner of free radicals, unsaturated groups (38), and labile hydrogen (72). A more general concept of the effect of structure of the hydrocarbon undergoing changes due to aluminum chloride or hydrogen chloride is in the weakening of the bond strengths in the hydrocarbon. This is supported by the fact that catalytic reactions are known in which hydrocarbons react in the presence of aluminum chloride alone or with added hydrogen chloride.

*While the theories given explain certain reactions, no one theory or mechanism is entirely adequate.*

## II. PARAFFINS

The paraffins in the presence of aluminum chloride form isomers, lower and higher paraffins, olefins, cycloparaffins, liquids of unknown constitution, carbon, and hydrogen, depending upon the original paraffin and the experimental conditions. In general, a key hydrocarbon in the form of butane results from treatment of higher paraffins.

Little work has been done on the first five members of this series, as shown in table 1. In some experiments, methane and ethane appeared to be inert (89), dissociating largely to carbon and hydrogen at high temperatures. Ethane, propane, *n*-butane, and isobutane yielded liquids. Propane reacted to give methane, ethane, and a heavy oil, whereas *n*-butane in the presence of hydrogen chloride and aluminum chloride formed lower paraffin and unsaturated hydrocarbons, besides some isobutane (79). *n*-Pentane reacted with aluminum chloride to give *n*-butane, isobutane, and isopentane, and the aluminum chloride surface was coated with a tarry (51) layer.

Hexane and higher paraffins dissociate principally to butanes, small amounts of propane and pentanes, and some higher paraffins. Although butane was the hydrocarbon given off in largest amounts, some workers reported *n*-butane and others isobutane. This may be due to an error in identification, but, as the data stand now, it appears that *n*-butane in some cases and isobutane in others, or both, are actually formed.

An examination of the quantities and kind of aluminum chloride reported indicates that when a low concentration (1 to 10 per cent) is used or water is added, isobutane predominates; when concentrations of 20 to 50 per cent are used, *n*-butane is obtained. These results should be carefully checked under comparable conditions. Besides gaseous hydrocarbons, the higher paraffins yield isomers, still higher paraffins, and unsaturated hydrocarbons. Again the appearance of isomers of the paraffins is linked with relatively low concentrations of aluminum chloride.

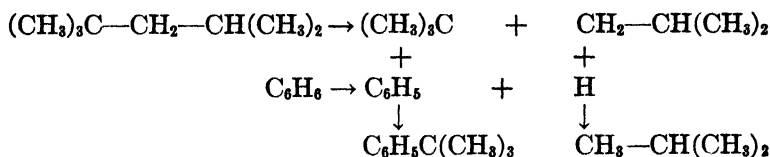
The following conclusions as a result of a study (100) of the action of

low concentrations of aluminum chloride upon *n*-hexane and *n*-octane have been made: (1) isomerization occurs; (2) isomerization by aluminum chloride is activated strongly by hydrogen chloride or substances readily giving off hydrogen chloride, such as alkyl chlorides and compounds of hydrogen chloride with anhydrous sulfates of heavy metals; (3) in the absence of hydrogen chloride, isomerization by aluminum chloride proceeds with considerable velocity only at increased temperature and with an induction period which corresponded to hydrogen chloride formation; and (4) an increase in exposed surface of aluminum chloride and stirring strongly accelerate the reaction of isomerization.

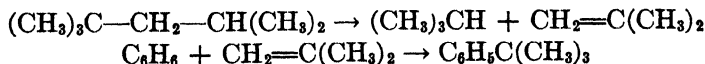
Paraffins react not only alone in the presence of aluminum chloride but also with a second hydrocarbon forming a higher one (50, 53, 80, 81).

Paraffins are alkylated by olefins and by cyclopropane, giving mainly higher paraffins. This work is shown in table 2. This reaction is similar to the alkylation of benzene, toluene, and xylenes by olefins.

A particularly interesting paraffin studied (53) is 2,2,4-trimethylpentane. When the reaction of this paraffin and benzene is catalyzed by aluminum chloride and hydrogen chloride, mono- and di-tertiary-butyl benzenes are obtained. Apparently the chain breaks into four-carbon atom radicals with a tertiary carbon atom. The tertiary carbon radical unites with a phenyl group, while the other unites with a hydrogen atom to give isobutane, as shown:



An alternate mechanism for the reaction involves the formation of an olefin and a paraffin from the starting paraffin. The olefin in turn reacts with the aromatic hydrocarbon, as illustrated.



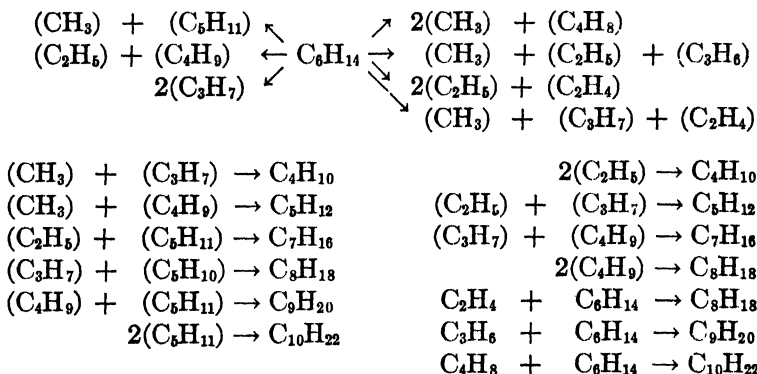
Unsaturated hydrocarbons have been found in the lower layer of the reaction mixture, and in certain cases aluminum chloride addition compounds with the unsaturates have been identified. The thermal reactions of gaseous paraffins are characterized by the formation of unsaturated hydrocarbons, while in the presence of aluminum chloride the reactions yield a layer of paraffins and a layer of unsaturates. This points to a preferential reaction of aluminum chloride for the weakening of the carbon-carbon bond, causing cleavage into two-carbon atom radicals and un-

TABLE 2  
*Reactions of paraffins with other hydrocarbons*

COMPOUNDS	TEMPERATURE °C.	TIME hours	CONCENTRATION OF $AlCl_3$ per cent	PRESSURE atm.	PRODUCTS		REFERENCES
					Gases	Liquids and solids	
iso- $C_4H_{10}$ + $C_2H_4$ + HCl	20-30	32-40	12	1	No	Higher paraffins; unsaturated hydrocarbons	(80)
iso- $C_4H_{10}$ + $C_2H_4$ + HCl	25	10	12	15		Paraffins (hexanes, octanes, decanes)	(81)
$n$ - $C_4H_{10}$ + $C_2H_4$ + HCl	29-33	15	10	1		Higher paraffins; cycloparaffins; unsaturated hydrocarbons	(81)
$n$ - $C_4H_{10}$ + $C_2H_4$ + HCl	25	36	10	15		Paraffinic hydrocarbons	(81)
iso- $C_4H_{10}$ + $C_2H_6$ + HCl	125	23	10	1	Propane	Alkylated benzenes	(80)
$n$ - $C_4H_{10}$ + $C_2H_6$ + HCl	100	17	10	1	Butane	Paraffins below hexane; alkylated benzenes (b.p. 90-200°C.)	(80)
2,2,4-( $CH_3$ ) <sub>3</sub> $C_4H_9$ + $C_2H_6$ + HCl	20-50	4	9	1	Isobutane; propane (trace); pentane	Tertiary-butylbenzene; unsaturated hydrocarbons	(53)
iso- $C_4H_{10}$ + cyclopropane + HCl	-30 to +30					Heptanes and higher paraffins	(54)

saturated carbon chains. The unsaturated chain or radical polymerizes, unites with a paraffin, or forms addition compounds with the aluminum chloride. The polymerization products of ethylene, such as hexene and octene, may rearrange to give cycloparaffins as they do in the thermal reactions of ethylene.

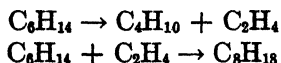
In the thermal reactions of gaseous paraffinic hydrocarbons, the weakest bond appears to be the carbon-carbon linkage. The work on the heats of combustion (116) of isomeric octanes gives a constant value for the carbon-carbon bond. It has been indicated (117) that for hexane and lower members of the series, the strength of the carbon-carbon bond and of the carbon-hydrogen bond is dependent on the position of the bond. It appears that these variations in bond strengths are small, and therefore do not seriously affect the assumption of constancy in the carbon-carbon bond. However, there are other indications that these variations may not be a negligible factor. In the thermal reactions of hydrocarbons there is a tendency for scissions in the carbon-carbon bonds with the formation of an unsaturated molecule with two carbon atoms (38). When most hydrocarbons react in the presence of aluminum chloride, butane is the principal gaseous product. This points to a scission of the chain into a unit with four carbon atoms or into units with two carbon atoms which combine to give butane. Less probable scissions along the chain do occur, as is evident from the appearance of propane and pentane. If hexane is taken as an example of a higher paraffin, the formation of paraffins may be represented in the following equations:



This explanation arises from the consideration that the energy necessary to cause the hydrocarbon to react is supplied in the case of thermal reactions by heat alone and in the case of catalytic reactions by the energy induced by aluminum chloride.

If the reaction is described in terms of the products, it would be stated

that the original paraffin forms a lower member and an olefin, while the olefin adds to another molecule of the original paraffin to give a higher member, as indicated by the reaction of hexane.



The mechanism is supported by the fact that olefins have been shown to alkylate paraffins, forming higher ones (see table 2).

Ethylene polymerizes to butene or higher olefins in the *absence* (37a, 38) of aluminum chloride. If ethylene is a reaction product of dissociation of the paraffin, it might polymerize to higher olefins before it alkylates part of the original paraffin. The greater tendency for the formation of paraffins rather than olefins in the presence of aluminum chloride indicates that higher paraffins form through the union of alkyl radicals rather than through a primary decomposition into olefins and subsequent addition to a paraffin. This is supported by the predominant appearance of the butanes in the gaseous products, even with a large variation in the nature of the original paraffin. The aluminum chloride increases the tendency for the scission of the carbon-carbon bonds into smaller units, and when present in small amounts or in the partially hydrated or hydroxy form, causes a shifting of carbon atoms within the molecule. Thus *n*-hexane gives some isobutane, methylcyclopentane, and hexane isomers; heptane yields isomeric heptanes. The variance in the form of butane obtained probably arises from isomerization of the *n*-butane into isobutane.

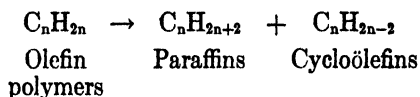
### III. OLEFINS

Olefins in the presence of aluminum chloride polymerize, isomerize, cyclicize, and form paraffins and more highly unsaturated compounds. Polymerization yields unsaturated liquid and solid products. Isomerization of olefins gives cycloparaffins, while polymerization followed by isomerization also yields cycloparaffins. Dehydrogenation may produce diolefins, which cyclicize to cycloolefins; or the cycloparaffins may dehydrogenate to the corresponding cycloolefins. Hydrogen from the latter reaction hydrogenates an olefin to a paraffin. Isomerization, polymerization, and dehydrogenation yield aromatic compounds. The gases formed are hydrogen, propane, and butane, the latter not so consistently as in the case of the paraffins. These products and reactions are similar to those observed in thermal reactions, except that a lower temperature is used, which gives a wider range to the type and size of molecules formed without decomposition taking place.

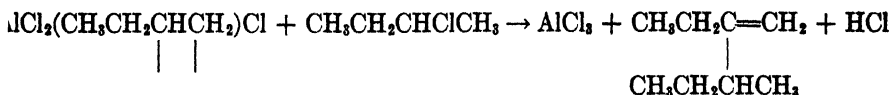
Subjecting ethylene (37a, 38) to temperatures of 350–400°C. causes a thermal polymerization to butene, hexene, and higher olefins. At slightly

higher temperatures scissions of carbon-carbon bonds occur along the chain of the olefins, giving two types of radicals which on hydrogenation form olefins and paraffins. Since the catalytic action of aluminum chloride appears to consist of the weakening of the bonds, these reactions should occur at lower temperature in its presence. It follows that in the catalytic reaction of ethylene, polymerization probably takes place first. This will be followed by scissions of the carbon-carbon bond in higher olefins, resulting in the formation of paraffins, owing to coupling of the alkyl radicals, and the formation of cycloolefins, owing to the combination of the unsaturated radicals. Ethylene is known to yield some cyclohexane when polymerized by heat; apparently ethylene polymerizes to hexene, which in turn cyclicizes.

The nature of the products from the polymerization of ethylene has been investigated by a number of experimenters (77, 119, 129). They found an upper layer of "free oil", paraffinic in character, and a lower layer of "combined oil", consisting of cycloolefins in combination with aluminum chloride. The polymerization of ethylene with aluminum chloride is accompanied therefore by dehydrogenation-hydrogenation reactions, so that the final products are not true polymers of ethylene. The term "conjunct polymerization" (77) has been suggested for such reactions, which can be represented as follows:



The polymerization of butene in the presence of aluminum chloride and hydrogen chloride has been reported to take place as follows (76a):

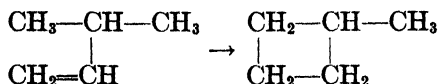


The octene decomposes into a paraffin and into a diolefin which cyclicizes readily.

It was found that the course of the polymerization of isobutene depends upon the temperature gradient (143). At room temperature the reaction with aluminum chloride is moderate, whereas a violent reaction takes place at  $-78^\circ\text{C}$ ., sometimes explosively. When 2-butene is treated with aluminum chloride at  $-10^\circ\text{C}$ ., a high yield of cycloparaffins (146) results.

Rapid polymerization of certain pentenes occurs even at  $-80^\circ\text{C}$ . in the presence of aluminum chloride (95). Amylene produced a resinous mass which, upon treatment with hydrochloric acid, resulted in the elimination of aluminum and the formation of a thick oil which yielded a

yellow oil and an asphaltic residue (41). Other experiments showed that cycloparaffins resembling lubricating oil, methylcyclobutane, and hexane were formed (5). The formation of methylcyclobutane indicates an isomerization by ring closure as indicated by the equation:



The polymers produced from 2-pentene and from 3-methyl-1-butene having a partly cyclic structure have been reported (140).

The effect of high aluminum chloride concentration was shown (40) by treating trimethylethylene at room temperatures for five weeks with an equal weight of aluminum chloride, producing *n*-pentane, isopentane, hexane, heptane, octane, and decane rather than heavy oils.

Ethylene, propene, isobutene, octene, and pentene form paraffins and cycloparaffin liquids when treated with aluminum chloride at 100° to 150°C. (134). Liquids with five to eight carbon atoms per molecule were formed from ethylene, propene, and butene when subjected for 0.5 to 100 seconds to temperatures up to 300°C. in the presence of aluminum chloride (76). These observations indicate that higher temperatures, approaching the point of thermal reactivity of the hydrocarbons themselves, are suitable conditions for the formation of products from olefins and aluminum chloride.

The lower olefins have been polymerized both in the absence (28, 52, 71, 108) and in the presence of a hydrocarbon which was considered an inert solvent (140, 142, 143, 144).

When olefins are heated from 100° to 200°C. in the presence of aluminum chloride at atmospheric pressure or at 20° to 100°C. with increased pressure (86) and in the absence of added solvents, two oily layers are formed. The oil in the upper layer has been called "free oil", and that in the lower layer "fixed" or "combined" oil. The latter may be freed from the aluminum chloride if the reaction mixture is poured over ice. The "free oil" may be decanted from the aluminum chloride sludge, which after refining is a "good lubricant." The "combined oil" after hydrolysis yields an inferior lubricant. Since these oils are better than the natural oils in quality, the reaction has been considered an important one. Patents have been issued for the production of oils and resins from olefins or cracked distillates (8, 22, 68, 71, 96, 97, 107, 113, 119, 136, 145).

Aluminum chloride suspended in petroleum ether or gasoline is capable of polymerizing ethylene, propene, butenes, and pentenes, forming a hydrocarbon mixture still containing olefin bonds (115). Such investigators as have considered petroleum ether or gasoline or certain paraffins as inert

solvents are in error, because paraffins have been shown to undergo (1) autodestructive alkylation and isomerization in the presence of aluminum chloride and hydrogen chloride (see table 1), and (2) alkylation by olefins in the presence of this catalyst (see table 2).

The aluminum chloride and the thermal (38) mechanisms indicate a directing force in the aluminum chloride reaction with olefins to form paraffins, cycloparaffins, or cycloolefins preferentially. With lower olefins the primary reaction is the polymerization to higher ones. Lubricating oils were produced by thermal polymerization of ethylene (8), completing the polymerization reaction by treatment with aluminum chloride at room temperature. The extent of polymerization depends on the size and structure of the olefin. From the thermal reactions of the gaseous olefins it appears that the more straight chain the molecule is, the less readily it will polymerize. It would be expected that these relationships hold even when aluminum chloride is present, and this appears to be borne out by the report that aluminum chloride polymerizes ethylene, propene, 1-butene, 2-butene, isobutene, 1-pentene, 2-pentene, 2-methyl-1-butene, 3-methyl-1-butene, trimethylethylene, 1-hexene, 1-octene, and cetene primarily into high-boiling liquids (133). The results of the experiments show that the more branched the olefin structure, the poorer the lubricating quality of the oil becomes, owing to the high change in viscosity as a function of temperature rise. The long-chain paraffin hydrocarbons are superior lubricants compared to the cycloparaffins, olefins, and aromatics. Since the viscosity factor of the oil is important, the paraffins produced should have large molecules. Starting with the lower olefins, polymerization should proceed slowly in order that long-chain molecules be built up; and it was found that the amount of paraffinic oil depended on the contact time (129).

Aluminum chloride weakens the bonds in the olefins, and if the hydrocarbons are treated to build higher paraffins, the action of the catalyst should not be so vigorous that the hydrocarbon molecule will split into small radicals. Therefore a low concentration is desirable, as shown by the use of 3 to 5 per cent aluminum chloride in the polymerization of olefins to lubricating oils. On the other hand, for the production of lower paraffins out of high-boiling fractions, a higher concentration of aluminum chloride is desirable. An inspection of table 3 indicates the nature of the reaction of olefins with aluminum chloride. Predominantly, there is a direct polymerization to higher olefins. Secondly, higher olefins by cyclization produce cycloparaffins. Finally, dehydrogenation-hydrogenation reactions change these cycloparaffins into cycloolefins, aromatics, or carbon (as products of dehydrogenation) and paraffins.



TABLE 3  
*Reactions of olefins*

COMPOUNDS	TEMPERATURES °C.	TIME hours	CONCENTRATION OF $\text{AlCl}_3$ per cent	PRODUCTS		REFERENCES
				Gases	Liquids and solids	
Ethylene + HCl . . . . .	100	1 week		$\text{C}_2\text{H}_4$ + HCl from crystal- line product	Complex compound, $\text{AlCl}_3 \cdot \text{C}_2\text{H}_4$	(58)
Ethylene + ethyl alcohol..	Room				Crystalline product, $\text{AlCl}_3 \cdot 3\text{C}_2\text{H}_5 \cdot \text{H}_2\text{O}$	(67)
Ethylene . . . . .	40-300	0.5-100 sec- onds	100 (at start)		Liquid hydrocarbons with five and more carbon atoms per molecule	(76)
Ethylene.....	20-30				Paraffins, 52.8 per cent; unsatu- rated cyclic hydrocarbons, 47.2 per cent	(77)
Ethylene.....	Room			Paraffins; ole- fins; hydrogen	Low-boiling paraffins; high-boil- ing cycloparaffins	(86)
Ethylene.....	200-280				Carbon	(86)
Ethylene + petroleum ether . . . . .	Room-100	4-12 days Short	16.7 (at start)		Paraffins; olefins; aromatics	(110)
Ethylene + gasoline .	Room				Unsaturated liquid hydrocarbons	(115)
Ethylene + petroleum ether. . . . .	Room	Few hours			Unsaturated liquid hydrocarbons	(115)
Ethylene.....	Room-180				Paraffins; cycloparaffins; olefins	(115)
Ethylene + naphtha . .	100-150				Polymerization product	(133)
Ethylene . . . . .					Low-boiling paraffins and higher boiling cycloparaffins	(134)
Propene + nitrobenzene..	Room	3 65	17 2 (at start)		Product of b. p. 80-200°C.	(39)

Propene + nitrobenzene...	50	0.5-100 seconds	100 (at start)	Butane + propane	Viscous oils	(39)
Propene + ethyl alcohol..	40-300				Crystalline product	(67)
Propene.....		Short			Liquid hydrocarbons with five and more carbon atoms per molecule	(76)
Propene + petroleum ether.....	Room				Unsaturated liquid hydrocarbons	(115)
Propene + naphtha..	150				Polymerization product, 33.3 per cent	(133)
Propene.....	10-30				Low-boiling paraffins and higher boiling cycloparaffins	(134)
Allene.....					High-boiling polymerization products	(75)
Butene + ethyl alcohol..	40-300	0.5-100 seconds	100 (at start)		Crystalline product	(67)
Butene.....					Liquid hydrocarbons with five and more carbon atoms per molecule	(76)
Butenes + petroleum ether.....	Room	Few hours	16.7 (at start)		Unsaturated liquid hydrocarbons, low-boiling paraffins and higher boiling cycloparaffins	(115)
1-Butene + naphtha.....					Polymerization product, 46.4 per cent	(133)
2-Butene + naphtha.....					Polymerization product, 33.3 per cent	(133)
2-Butene.....	-10	2	1.75		Cycloparaffins, 92.9 per cent	(146)
Isobutene + nitrobenzene.			17.2 (at start)		Product of b.p. 60-190°C.	(39)
Isobutene + benzene + diphenylsulfone... ..	Room	4.1	8.33 (at start)		Diisobutene; triisobutene; higher polymerization products	(39)
Isobutene + nitro-methane.....	0				Very viscous oil	(39)
Isobutene + naphtha.....					Polymerization product, 42.0 per cent	(133)

TABLE 3—Continued

COMPOUNDS	TEMPERATURE °C.	TIME hours	CONCENTRATION OF $AlCl_3$ per cent	PRODUCTS		BROMINE INDEX
				Gases	Liquids and solids	
Isobutene.....	100-150				Low-boiling paraffins; higher boiling cycloparaffins	(134)
Isobutene + pentane.....	-78	2	5.26		Very viscous polymer of high molecular weight	(143)
Isobutene + pentane.....	-35 to -40	2	5.26		Polymerization product	(143)
Isobutene + pentane.....	+7 to +16	2	3.23		Polymerization product	(143)
Butadiene .....		Slow			Polymerization product	(151)
Amylene + ethyl alcohol..					Crystalline product	(67)
Amylene. ....	Room				Viscous yellow oil and asphaltic residue	(41)
Amylene + petroleum ether .....	Room	Short			Unsaturated liquid hydrocarbons	(115)
Amylene.....	0-20	5 weeks	50	Unidentified gas	Cycloparaffins resembling lubricating oil; unidentified hexane; methylcyclobutane	(5)
1-Pentene + naphtha... ..					Polymerization product, 59.8 per cent	(133)
1-Pentene.....	-80	5½			Polymerization product, small yield	(95)
2-Pentene. ....	-80	5½			Polymerization product, small yield	(95)
2-Pentene .....	Room	Short			Polymers	(95)
2-Pentene + HCl. ....	-80				2- and 3-chloropentanes, 40 per cent; hydrochlorides of alkenes of polymerization, 60 per cent	(95)
2-Pentene + naphtha.....					Polymerization product, 38.5-53.0 per cent	(133)

2-Pentene.....	0				Polymers with a partly cyclic structure	(140)
2-Methyl-1-butene + naphtha					Polymerization product, 34.5 per cent	(133)
2-Methyl-1-butene + HCl.	-80				2-Chloro-2-methylbutane; hydrochlorides of alkenes of polymerization	(95)
2-Methyl-1-butene.	-80	5½			Polymers, 49 per cent	(95)
2-Methyl-2-butene + naphtha					Polymerization product, 29.3 per cent	(133)
2-Methyl-2-butene..	Room	5 weeks	50		Pentane; isopentane; hexane; heptane; octane; decane	(40)
2-Methyl-2-butene.....	-80	5½			Polymers, 82 per cent	(95)
2-Methyl-2-butene + HCl.	-80				2-Chloro-2-methylbutane; hydrochlorides of alkenes of polymerization	(95)
3-Methyl-1-butene + naphtha.....					Polymerization product, 50.8 per cent	(133)
3-Methyl-1-butene.....	-80	Very slow			Alkenes of polymerization	(94)
3-Methyl-1-butene.....	-80	44			Polymers, 60 per cent	(95)
3-Methyl-1-butene + HCl.	-80				Hydrochlorides of alkenes of polymerization, 60 per cent; 2-chloro-3-methylbutane, 20 per cent	(94)
3-Methyl-1-butene + benzene.....	85				Polymers with a partly cyclic structure	(140)
3-Methyl-1-butene + benzene.....	200				Polymers with a partly cyclic structure	(140)

TABLE 3—*Concluded*

COMPOUNDS	TEMPERATURE °C.	TIME hours	CONCENTRATION OF $AlCl_3$ per cent	PRODUCTS		YIELD, PERCENT
				Gases	Liquids and solids	
Isoprene .....	151	24			White, soft polymer	(151)
Isoprene + nitrobenzene..					Soluble polymer of isoprene	(137)
Isoprene + ethyl acetate..					Soluble and insoluble polymers	(137)
Isoprene + HCl.....					Soluble and insoluble polymers	(137)
Isoprene.....	Room	Slow			Insoluble polymer	(137)
Isoprene + 2-pentene ..					Insoluble polymer and one soluble polymer of isoprene	(137)
Isoprene.....	Room	Few minutes			Polymer of high molecular weight	(6)
"Commercial" isoprene....		24			Insoluble and soluble solids of unsaturated character	(7)
Isoprene.....					Yellow flaky polymer	(148)
Isoprene + benzene....					Polymers of isoprene	(21)
Isoprene + pentene.....					Amorphous condensation product	(6)
Isoprene + 2-methyl-2-butene.....					Amorphous condensation product	(6)
1-Hexene + naphtha....					Polymerization product	(133)
2,3-Dimethylbutadiene...		24			White, soft polymer	(151)
1-Octene + naphtha.....					Polymerization product	(133)
Octene.....	100-150				Low-boiling paraffins and higher boiling cycloparaffins	(134)
Diamylene .....	150			Butane + propane	Low-boiling paraffins and higher boiling cycloparaffins	(134)
Cetene.....	57.2				Polymerization product, 85.0 per cent	(133)

## IIIA. DIOLEFINS

Diolefins are polymerized in the presence of aluminum chloride. It is reported that allene (75) yields products of polymerization by contact with aluminum chloride at room temperature and below. Various polymerization products have been obtained from the action of aluminum chloride on butadiene, isoprene, and 2,3-dimethylbutadiene (151). Isoprene yields a high molecular weight hydrocarbon in the presence of aluminum chloride, and upon standing soft white, flaky yellow, soluble, or insoluble polymers are formed, depending upon the conditions of the reaction (6, 7, 148).

Solvents have an important influence on the degree of polymerization of isoprene (137). Any solvent in which isoprene and aluminum chloride were mutually soluble favored the formation of soluble polymers. Pure isoprene underwent a slow polymerization to insoluble polymers in the presence of aluminum chloride at room temperature. Addition of dry hydrogen chloride to the isoprene led to both soluble and insoluble polymers, probably owing to the presence of the solvent-like hydrochloride of isoprene which was also formed.

## IV. ACETYLENES

A complex compound which acetylene forms with aluminum chloride has been isolated and identified and is relatively unstable (67). Acetylene was absorbed by anhydrous aluminum chloride even in the cold (12). At 70°C., the acetylene is absorbed in a few minutes to give a reddish sublimate, which becomes black as more acetylene is absorbed at 120–130°C.

It has been reported (75) that allylene and diacetylene yield products of polymerization by contact with aluminum chloride at room temperature and below.

Vinylacetylene treated at 50–110°C. with less than 2 per cent of aluminum chloride yields unsaturated polymers of non-benzenoid character (25).

The reactions of the acetylenes with aluminum chloride are summarized in table 4. Reactions of acetylene in the presence of aromatics and aluminum chloride are considered in table 14.

## V. CYCLOPARAFFINS

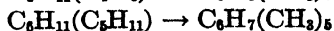
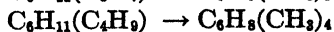
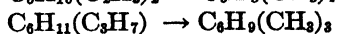
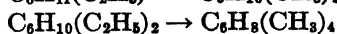
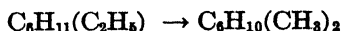
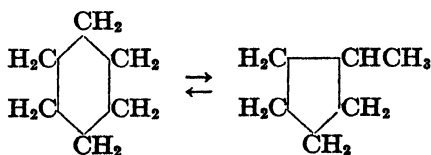
Cycloparaffins isomerize and dehydrogenate readily. Alkyl side chains of two more carbon atoms rearrange to methylate the cycloparaffin. Polycyclization takes place by dehydrogenation or isomerization. In general, butane, with higher and lower paraffins and olefins, is formed from the reaction of cycloparaffins and aluminum chloride.

Cyclopentane and cyclohexane were found to be stable below 60°C. with aluminum chloride. In the presence of water at somewhat higher temperature cyclohexane isomerized into methyleyclopentane. The for-

TABLE 4  
*Reactions of acetylenes*

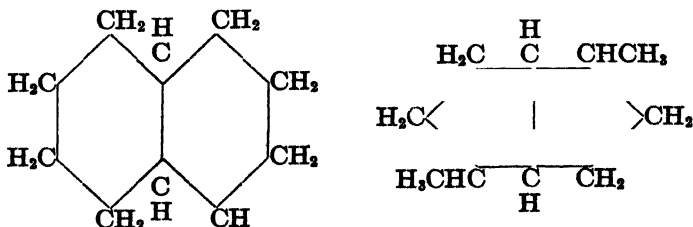
COMPOUNDS	TEMPERATURE	TIME	CONCENTRATION OF $\text{AlCl}_3$	PRODUCTS		REFERENCES
				Gases	Liquids and solids	
Acetylene.....	60-62	5 days	100 per cent	Dense fumes $\text{C}_2\text{H}_2$ + $\text{HCl}$ from the crystalline product	Reddish-brown sublimate	(67)
Acetylene + ethyl alcohol..	Room				Colorless crystals of $\text{AlCl}_3 \cdot 2\text{C}_2\text{H}_2 \cdot 2\text{H}_2\text{O}$	(67)
Acetylene.....	70	Few minutes	100		Red sublimate, $(\text{C}_{10}\text{H}_{18}\text{O})_7 \cdot \text{Al}_2\text{Cl}_6$	(12)
Acetylene.....	120-130		100		Black substance, $(\text{C}_7\text{H}_{11})_7 \cdot \text{Al}_2\text{Cl}_6$	(12)
Allylene.....	10-30				High-boiling polymerization products	(75)
Vinylacetylene.....	50-110		<2		Unsaturated polymers of non-benzoid character	(25)
Diacetylene.....	10-30				High-boiling polymerization products	(75)
Pentynes + nitromethane...	20		19.8		Viscous oil	(39)

mation of isobutane (82), as well as dicyclohexyl, *m*-dimethylcyclohexane, and dimethyldicyclopentyl, was observed at 150°C. when cyclohexane was treated with aluminum chloride. In the presence of an acceptor for hydrogen such as arsenic chloride, di- and tri-cyclohexyl were obtained from cyclohexane (105). Working with alkylated cyclohexanes it was found that the *o*- and *p*-dimethylcyclohexanes gave the meta form. This preference for the meta form was observed also with aromatics. Ethylcyclohexane when heated with aluminum chloride gave dimethylcyclohexane; and the diethylcyclohexanes yielded di- or tetra-methyl compounds. This is especially interesting, since the alkyl group as a side chain has been ruptured within the chain. Scission in the side chain and distribution of the methyl group around the cyclohexane ring is a function of the size of the original alkyl group. Thus, propylcyclohexane yielded trimethylcyclohexane, butylcyclohexane produced tetramethylcyclohexane, and amylcyclohexane was converted into pentamethylcyclohexane; in addition to the methylcyclohexanes, *n*-butane was reported in all cases except from isoamylcyclohexane, when some isobutane was formed. If a fairly high concentration of aluminum chloride was used, the resulting vigorous exothermic reaction probably removed *n*-butane before any isomerization to isobutane occurred. Some reactions of the cycloparaffins are shown in the following equations:



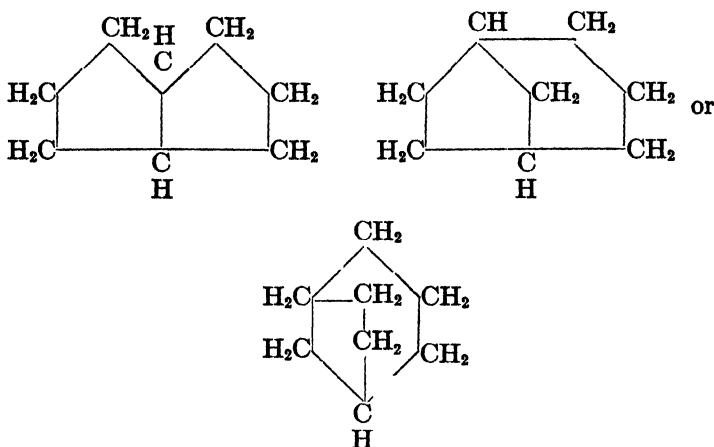
Decalin and aluminum chloride at 130°C. gave cyclohexane, methylcyclohexane, and 1,3,5-trimethylcyclohexane (88) in small amounts; however at 150°C. charring occurred.

*trans*-1,4-Dimethylbicyclo(0,3,3)octane was also isolated, indicating a transformation of cyclohexane rings into methylcyclopentane rings, as follows:

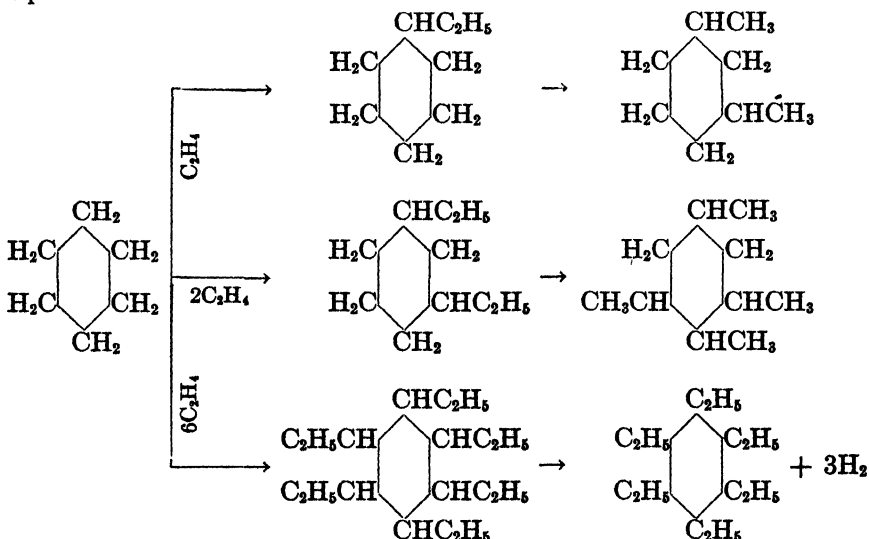




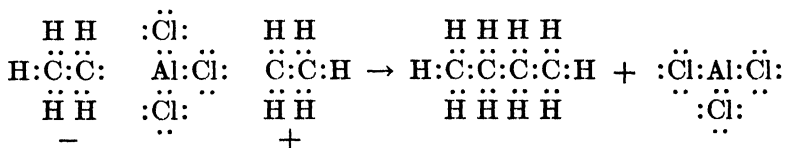
Cyclopentane rings can also be converted into cyclohexane rings, as shown (11) by the conversion of *cis*-bicyclo(0,3,3)octane into bicyclo(1,2,3)octane:



In the reaction of cyclohexane and ethylene in the presence of aluminum chloride, which has been studied (83), the action of the alkylated cyclohexanes and the relation of these to hexaethylbenzene is shown in table 6. Instead of ethyl- or diethyl-cyclohexane forming, as would be expected from other ethylating reactions, *m*-dimethyl- and 1,3,4,5-tetramethyl-cyclohexane were formed; instead of hexaethylcyclohexane, hexaethylbenzene resulted. These reactions may be represented by the following equations:



Butane is usually the gaseous hydrocarbon formed, except in the case of propylcyclohexanes, where propane results. Butane formed by the ethylated cyclo compounds probably results from the union of two ethyl radicals. From the amylcyclohexane, butane formation appears from a scission of the carbon-carbon bond within the side chain. The preference for the formation of a four-carbon atom paraffin in the reaction of pure hydrocarbons with aluminum chloride and the formation of the two-carbon atom olefin which occurs on thermal treatment find an explanation in the mechanism of the two reactions. Aluminum chloride weakens the bonds, making the simple scission into alkyl groups possible at low temperatures at which butane is stable, while in the thermal case butane is not readily formed. The preferential formation of butane can be ascribed to the building-up tendency of complexes of aluminum chloride with two-carbon atom molecules, as shown:



In contrast to the splitting-off of the whole alkyl group from the benzene ring, is the splitting within the side chain of the alkylated cyclohexanes, giving the methylated cyclohexanes. It will be shown that for aromatic compounds the weakest carbon-carbon bond is the one between the ring and side chain and not within the side chain as might be expected. The benzene ring appears to exert a repulsive force on the side chain, indicating that the unsubstituted benzene ring is the most stable form. This repulsive force must result from the nature of the benzene ring, since it is not observed, at least to the same degree, with the cycloparaffin rings. In the cycloparaffin compounds the difference in the strengths of these bonds had decreased so that both scissions occur.

The detailed data of cycloparaffin reactions are given in tables 5 and 6.

## VI. CYCLOOLEFINS

Relatively few experiments have been conducted with cycloolefins and aluminum chloride. Cycloolefins isomerize, polymerize, hydrogenate, and dehydrogenate and react readily with other hydrocarbons such as aromatics and aluminum chloride.

When cyclohexene was treated at 70°C., high molecular weight polymers (133, 142) were produced; another experimenter (142), operating at a temperature of -78°C. in the presence of hydrogen chloride, aluminum chloride, and pentane, found chlorinated cyclohexane and polycyclohexyl.

TABLE 5  
Reactions of cycloparaffins

COMPOUNDS	TEMPERATURE °C.	TIME hours	CON- CEN- TRA- TION (% $\text{AlCl}_3$ )	PRODUCTS		REFER- ENCES
				Gases	Liquids and solids	
Cyclopentane.....	60	8	23		No change	(34)
Methylcyclopentane ..	65-70	30	25		Cyclohexane (equilibrium mixture)	(103)
Cyclohexane.....	65-70	16	25*		Methylcyclopentane	(103)
Cyclohexane.....	100	72	25	HCl	Methylcyclopentane	(5)
Cyclohexane .....	100	24	50		Methylcyclopentane; dimethylcyclo- butane	(153)
Cyclohexane. ..	135-145	8-8	14†		No change	(52)
Cyclohexane + HCl.....	150	24	10	Isobutane	Methylcyclopentane; dicyclohexyl; dimethyldicyclopentyl; <i>m</i> -dimeth- ylcyclohexane	(52)
Cyclohexane + $\text{AsCl}_3$ .....	65-70	16	16†	HCl	Dicyclohexane; tricyclohexane	(105)
Methylcyclohexane .....	140-150	3	9†		No change	(52)
Methylcyclohexane ..	120-130		10		Hexamethylene; pentamethylene; paraffins	(138)
<i>o</i> - or <i>p</i> -Dimethylcyclohexane.....	115-120	7	23	Trace of gas	<i>m</i> -Dimethylcyclohexane	(52)
<i>m</i> -Dimethylcyclohexane.....	115-120	7	23	Trace of gas	Traces of unsaturated hydrocarbons	(52)
Dimethylcyclohexane.....	120-130		10		Hexamethylene; pentamethylene; paraffins	(138)
Ethylcyclohexane.....	115-120	8	21	Gas (small); ethane	<i>m</i> -Dimethylcyclohexane	(52)
Ethylcyclohexane.....	135-140				<i>m</i> -Dimethylcyclohexane	(138)
<i>m</i> -Diethylcyclohexane ..	120-130	4	23	Butane (small)	Tetramethylcyclohexane; polymer- ized cyclohexene	(52)
<i>m</i> -Diethylcyclohexane ..	100-130	1-2	20	No gas	Dimethylcyclohexane	(52)
<i>m</i> -Diethylcyclohexane ..	115-120	4	20	Butane	Dimethylcyclohexane	(52)

<i>m</i> -Diethylcyclohexane..	115-120	5	50	Butane (largest)	Dimethylcyclohexane	(52)
<i>n</i> -Propylcyclohexane....	135-145	7 5	30	Propane	Trimethylcyclohexane	(52)
Isopropylcyclohexane.....	130-145	7	23	Propane	Trimethylcyclohexane	(52)
<i>n</i> -, <i>sec</i> -, or <i>tert</i> -Butylcyclohexane ....	150-160	8	20-23	Butane (secondary, large; tertiary, small)	Tetramethylcyclohexane; liquid (b.p. 155-165°C.)	(52)
Amylcyclohexane.....	130-155	7	25	Butane	Isoamylcyclohexane; methyl- and tetramethyl-cyclohexanes	(52)
Isoamylcyclohexane....	130-140	5	17	<i>n</i> -Butane and isobutane	Pentamethylcyclohexane; methyl- and tetramethyl-cyclohexanes	(52)
Cycloheptane.....	100-300	3 days	55	Isobutane; <i>n</i> -butane		(152)
<i>cis</i> -Bicyclo-(0,3,3)-octane .....	Room	48	28 6		Bicyclo-(1,2,3)-octane	(11)
Decalin, 75 per cent <i>trans</i> .....	130		24 2		Cyclohexane; methylcyclohexane; 1,3,5-trimethylcyclohexane; 1,4-dimethylbicyclo-(0,3,3)-octane	(88)
<i>cis</i> -Decalin.....	100	12	24.3		<i>trans</i> -Decalin	(153)
<i>cis</i> -Decalin.....	Room	22	28.6		<i>trans</i> -Decalin	(153)

Added water (0.6 per cent)

Under pressure.

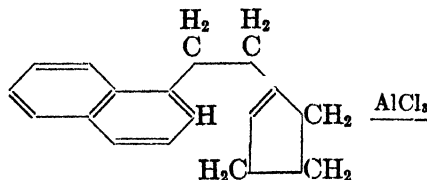
22 per cent of AsCl<sub>3</sub> present

TABLE 6  
*Reactions of cycloparaffins with ethylene*

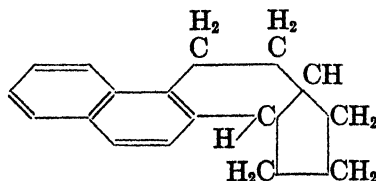
COMPOUNDS	TEMPERATURE	TIME	CONCENTRATION OF $\text{AlCl}_3$	PRODUCTS		REFERENCES
				Gases	Liquids and solids	
Cyclohexane + ethylene + HCl . . . . .	°C.	hours	per cent			
	50-60	13	11 1	Ethane	<i>n</i> -Dimethylcyclohexane; tetramethylcyclohexane; hexaethylbenzene	(83)
Methylcyclohexane + ethylene..	70	10			Cycloparaffins (b.p. 110°C. and up)	(83)
Methylisopropylcyclo- hexane + ethylene .	80	2 5			Cycloparaffins (b.p. 175°C. and up)	(83)

The reactions of cyclohexene in the presence of aromatic hydrocarbons (table 16) give cyclohexyl derivatives (16, 18).

The treatment of 1-( $\beta$ -1'-naphthylethyl)cyclo-1-pentene in carbon disulfide solution with aluminum chloride produced 1,2-cyclopentano-1,2,3,4-tetrahydrophenanthrene (31). In this reaction, ring closure upon an active double bond occurs, and the cyclization is represented as follows:

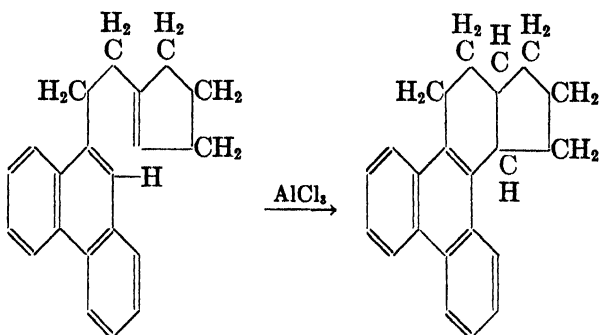


1-( $\beta$ -1'-Naphthylethyl)cyclo-1-pentene

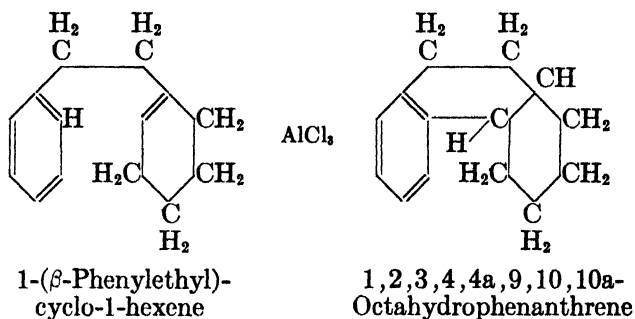


1,2-Cyclopentano-1,2,3,4-tetrahydrophenanthrene

In like manner 1-( $\beta$ -9-phenanthrylethyl)cyclo-1-pentene was treated in carbon disulfide solution with aluminum chloride at room temperature, giving tetrahydrocyclopentenotriphenylene (14) as indicated in the following equation:

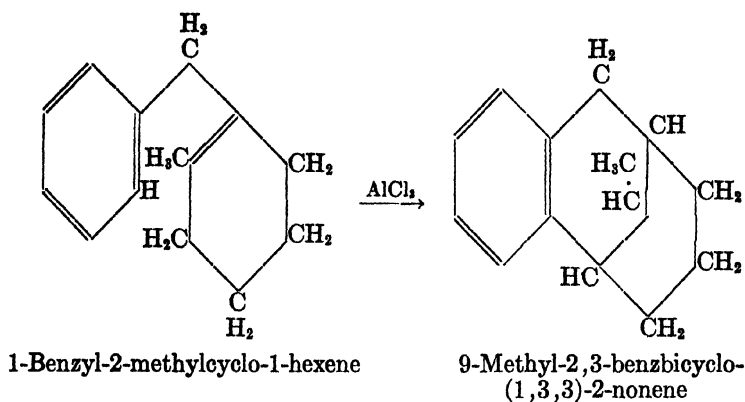


The compound 1-( $\beta$ -phenylethyl)cyclo-1-hexene was treated in carbon disulfide solution with aluminum chloride; this yielded 1,2,3,4,4a,9,-10,10a-octahydrophenanthrene (29, 31) according to the equation shown:

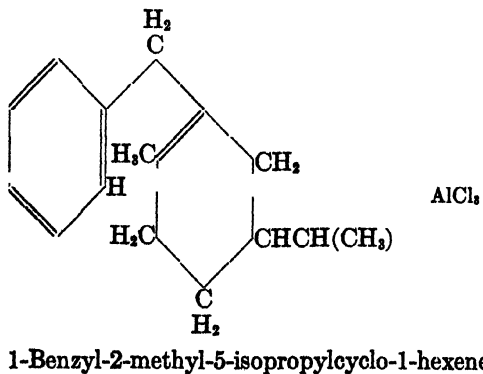
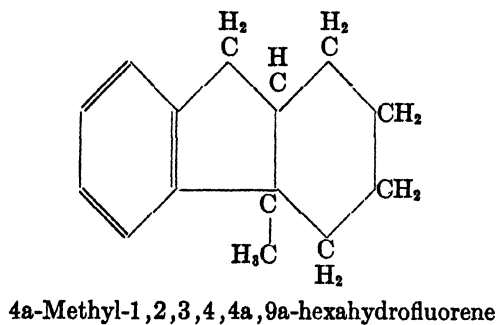


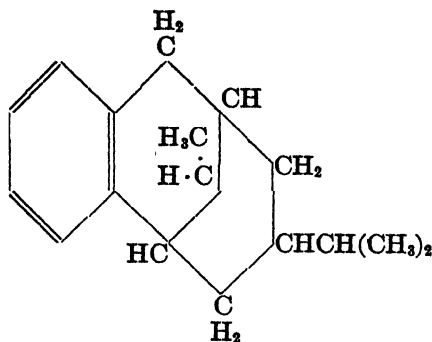
In these syntheses an isomerization of the unsaturated chain to a six-carbon atom ring structure occurs as a result of the action of aluminum chloride upon the double bond of a cycloolefin. The analogous alkylation of aromatics with olefins is discussed in section XI.

The compounds 1-benzyl-2-methylcyclo-1-hexene and 1-benzyl-2-methyl-5-isopropylcyclo-1-hexene, when treated with aluminum chloride at  $0^\circ\text{C}$ ., gave hydrocarbons of the same empirical formulas but without an active olefin bond (32). It was shown that the cyclization products cannot be hexahydrofluorenes, although it was not demonstrated that benzobicyclononenes are formed. Apparently, in this synthesis, closure to a six-carbon atom ring structure rather than to a five-carbon atom ring is favored by aluminum chloride, as indicated in the equations:

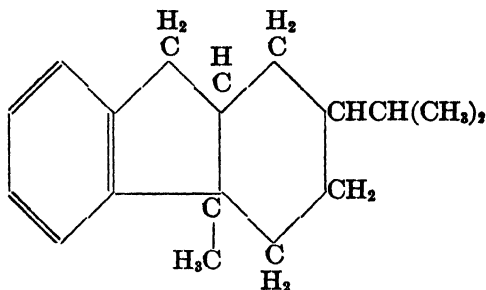


rather than





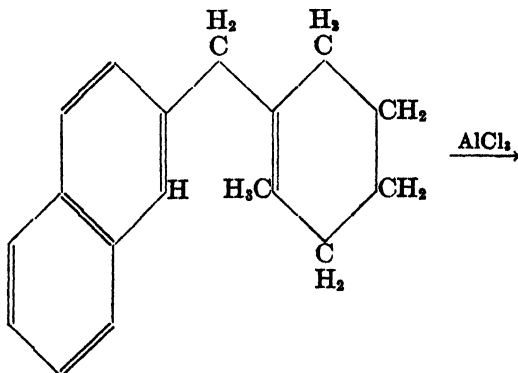
7-Isopropyl-9-methyl-2,3-benzbicyclo(1,3,3)-2-nonane  
rather than



2-Isopropyl-4a-methyl-1,2,3,4,4a,9a-hexahydrofluorene

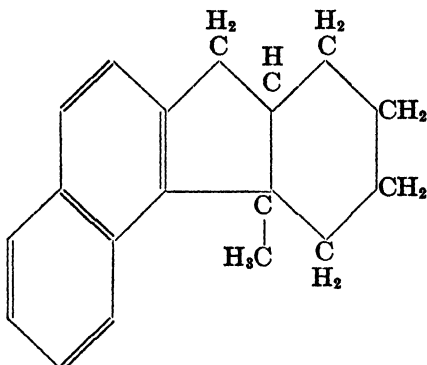
Apparently the strainless benzbicyclononene system is formed in preference to the hexahydrofluorenes after an initial isomerization of cyclo-1-hexenes to cyclo-2-hexenes.

The compound 1-methyl-2-(2'-naphthylmethyl)cyclo-1-hexene was treated in carbon disulfide solution with aluminum chloride, giving 7a,8,9,10,11,11a-hexahydro-11a-methyl-3,4-benzofluorene (28), as follows:



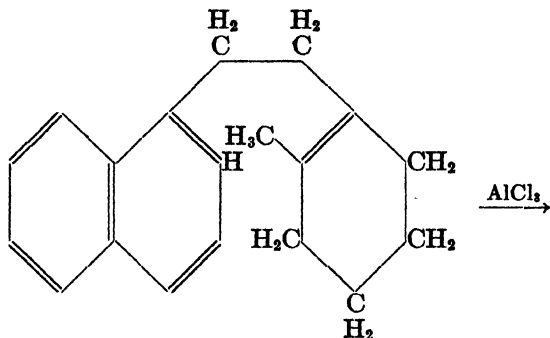
1-Methyl-2-(2'-naphthylmethyl)cyclo-1-hexene



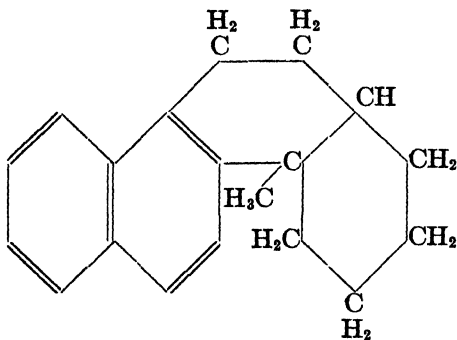


7a,8,9,10,11,11a-Hexahydro-11a-methyl-3,4-benzofluorene

The substance 1-( $\beta$ -2-methyl- $\Delta^1$ -cyclohexenylethyl)naphthalene was subjected to treatment in carbon disulfide solution with aluminum chloride, giving 1,2,2a,3,4,5,6,6a-octahydro-6a-methylchrysene (30):

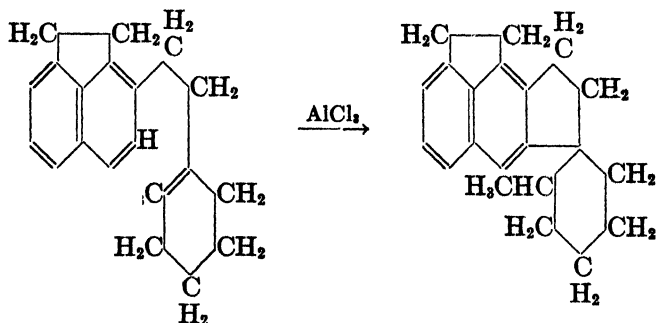


1-( $\beta$ -2-Methyl- $\Delta^1$ -cyclohexenylethyl)naphthalene  
(i.e., 2-methyl-( $\beta$ -1'-naphthylethyl)cyclo-1-hexene) .



1,2,2a,3,4,5,6,6a-Octahydro-6a-methylchrysene

The investigations showed that substitution of acenaphthyl for naphthyl in the previous cyclohexene derivative leads to formation of a spiran, as follows:



1-(β-2-Methyl-Δ¹-cyclohexenylethyl)-  
acenaphthene (i.e., 2-methyl-  
(β-1'-acenaphthylethyl)-  
cyclo-1-hexene)

8,9-Dihydro-2'-methylspiro-  
(β-acenaphthindan-3,1'-  
cyclohexane)

The general principle of cyclization for the naphthalenes and related hydrocarbons with cyclopentenylethyl, cyclohexenylethyl, or cyclohexenylmethyl groups in the alpha and beta positions, as considered in this section, is stated thus:—the cyclization of the alpha-substituted naphthalenes and related compounds and of the analogous monosubstituted benzene produces six-carbon atom rings. Cyclization of beta-substituted naphthalenes and related hydrocarbons produces five-carbon atom rings (72).

The details of the reactions in this section and those involving cyclohexadienes are given in tables 7 and 16.

## VII. TERPENES

The reactions of terpenes catalyzed by aluminum chloride result in the formation of polymers and of hydrogenated and chlorinated compounds. Paraffins, cycloparaffins, olefins, polyolefins, polynaphthenes, dihydropinene, and benzene are types of the products formed. The reactions are summarized in table 8.

The simultaneous action of aluminum chloride and iodine, which acted as an activator of the aluminum chloride upon pinene (44), produced pinene hydrochloride and iodides of pinene. The presence of pinene hydrochloride indicates that hydrogen chloride is produced by the action of aluminum chloride on the terpenes, and probably has an important function in the polymerizations of the terpenes.

When pinene, dipentene, sylvestrene, camphene, and isopinene reacted

TABLE 7  
Reactions of cycloolefins

COMPOUNDS	TEMPERATURE	TIME	CONCENTRATION OF $\text{AlCl}_3$	PRODUCTS		REFERENCES
				Gases	Liquids and solids	
1-( $\beta$ -1'-Naphthylethyl)cyclo-1-pentene + $\text{CS}_2$	0	24	8.13		1,2-Cyclopentano-1,2,3,4-tetrahydrophenanthrene, 83% ( <i>cis</i> + <i>trans</i> )	(31)
1-( $\beta$ -9-Phenanthrylethyl)cyclo-1-pentene + $\text{CS}_2$	Room	12			Tetrahydrocyclopentenotriphenylene	(14)
Cyclohexene					Polymerization product	(133)
Cyclohexene + pentane + $\text{HCl}$	-78	2 5	<10		Chlorocyclohexane, 50%; chloropoly-cyclohexyl compounds	(142)
Cyclohexene	70	7	6-7		High molecular polymers	(142)
1,3-Cyclohexadiene	Warmed				Polymerization product	(151)
1,4-Cyclohexadiene	Warmed				Partly hydrogenated product of polymerization; benzene	(151)
1-( $\beta$ -Phenylethyl)cyclo-1-hexene + $\text{CS}_2$		24	37 8		1,2,3,4,4a,9,10,10a-Octahydraphenanthrene, 85%	(31)
1-( $\beta$ -Phenylethyl)cyclo-1-hexene + $\text{CS}_2$	Room	6			1,2,3,4,4a,9,10,10a-Octahydraphenanthrene	(29)
1-Benzyl-2-methylcyclo-1-hexene	0	3	62		Methylbenzycyclononene, 70%	(32)
1-Benzyl-2-methyl-5-isopropylcyclo-1-hexene	0	5			Methylisopropylbenzycyclononene, 75%	(32)
1-Methyl-2-(2'-naphthylmethyl)cyclo-1-hexene + $\text{CS}_2$	0	6	6.8		7a,8,9,10,11,11a-Hexahydro-11a-methyl-3,4-benzofluorene, 47%	(28)
1-( $\beta$ -2-Methyl-4'-cyclohexenylethyl)-naphthalene + $\text{CS}_2$	0	7	8.7		1,2,2a,3,4,5,6,6a-Octahydro-6a-methylchrysene, 60%	(30)
1-( $\beta$ -2-Methyl-4'-cyclohexenylethyl)-acenaphthene + $\text{CS}_2$	0	21	7.3		8,9-Dihydro-2'-methyl-spiro-( $\beta$ -acenaphthindan-3,1'-cyclohexane)	(30)

TABLE 8  
*Reactions of terpenes*

COMPOUND	TEMPERATURE	TIME	CONCENTRATION OF $AlCl_3$	PRODUCTS		REFERENCES
				Gases	Liquids and solids	
L-Pinene.....	°C. 0 to room	hours 1	per cent 33 33		Brittle solid polymer ( $C_{15}H_{24}$ ) <sub>x</sub> of m.p. 77-78°C.; liquid	(130)
Pinene.....	Room		*		Pinene hydrochloride; iodides of pinene	(44)
Finnish turpentine oil (b.p. 160-167°C.).....	Room			Methyl and ethyl chlorides	Paraffin, olefin, polyolefin, and cycloparaffin mixture	(118)
Finnish crude turpentine.....	Room				Semisolid pitchy substances	(118)
French turpentine oil.....	Room	1-25 days	20-33 33		Solid or semisolid polymers	(45)
French turpentine oil.....	0 to room	16	30 33		Brittle solid polymer ( $C_{15}H_{24}$ ) <sub>x</sub> of m.p. 77-78°C.; liquid	(130)
French turpentine oil.....	Heated	2	25	Paraffins + cycloparaffins	Liquid, 63 per cent, containing pentane, isopentane, trimethylethylmethane, cyclooctane, cyclodecane, polynaphthenes, dihydropinene, benzene, and unsaturates	(130)
Sumatra turpentine oil (b.p. 156.8-157.2°C.) + pentane.	-15		15-25		Colorless oil of molecular weight 300; resin of molecular weight 500 to 600	(141)
Turpentine.....					Polymerization product	(133)
Pinene + isoprene.....					Amorphous condensation product	(6)
Dipentene + isoprene.....					Amorphous condensation product	(6)
Isopinene + isoprene.....					Amorphous condensation product	(6)
Camphene + isoprene.....					Amorphous condensation product	(6)
Sylvestrene + isoprene.....					Amorphous condensation product	(6)

\* Iodine present also.

TABLE 9  
*Reactions of benzene and methylbenzenes*

COMPOUNDS	TEMPERATURE °C.	TIME hours	CON- CENTRA- TION OF AlCl <sub>3</sub> per cent	PRESSURE atmospheres	PRODUCTS		REFERENCES
					Gases	Liquids and solids	
C <sub>6</sub> H <sub>6</sub> .....	180-200	48	17	Sealed tube		Toluene; ethylbenzene; diphenyl	(47)
C <sub>6</sub> H <sub>6</sub> .....	100	10-14 days	20	Sealed tube		Toluene; xylene; mono- and di-ethylbenzenes	(70)
C <sub>6</sub> H <sub>6</sub> .....	80	24	10		HCl	Tar; phenol, 1 per cent; benzene, 92 per cent	(101)
C <sub>6</sub> H <sub>6</sub> + HCl..	100	Many		Sealed tube		1-Methyl-3-phenylcyclopentane; diphenylcyclohexane	(64)
C <sub>6</sub> H <sub>6</sub> + HCl...						Complex compound, AlCl <sub>3</sub> ·3C <sub>6</sub> H <sub>6</sub>	(55)
C <sub>6</sub> H <sub>6</sub> .....	20	20 weeks	12 5*			Phenylcyclohexane; diphenyl; <i>o</i> -diphenylcyclohexane; cyclohexane; phenylmethylcyclopentane	(147)
C <sub>6</sub> H <sub>6</sub> + HCl.....	125	24	10	Under pressure		Ethylbenzene; diphenyl, 0.84 per cent; unsaturated oil; unsaturated ethylene polymers	(82)
C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub> .....	200	36-48	25	Sealed tube		Xylene; <i>o</i> - and <i>p</i> -ethyltoluenes; ditolyl	(47)
C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub> .....	111	3	20	Sealed tube		Benzene; <i>m</i> - and <i>p</i> -xylenes	(3, 4)
C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub> .....	111	Several	9			Benzene; <i>m</i> - and <i>p</i> -xylenes; higher methylated benzenes; dimethylanthracene	(93)
C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub> .....	111	24	10		HCl	Benzene; xylene; hexahydrotoluene	(101)
C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub> + HCl...						Complex compound, AlCl <sub>3</sub> ·3C <sub>6</sub> H <sub>5</sub>	(55)

$m\text{-C}_6\text{H}_4(\text{CH}_3)_2 + \text{HCl}$									(60)
$m\text{-C}_6\text{H}_4(\text{CH}_3)_2 \dots$	110-119	Few	20					Complex compounds, $2\text{AlCl}_3 \cdot \text{C}_6\text{H}_4(\text{CH}_3)_2$ and $2\text{AlCl}_3 \cdot 5\text{C}_6\text{H}_4(\text{CH}_3)_2$	(3, 4)
$m\text{-C}_6\text{H}_4(\text{CH}_3)_2$	135	4	16 7				$\text{CH}_3\text{Cl}$	Benzene; toluene; mesitylene; pseudocumene; durenene; isodurene	(87)
$\text{C}_6\text{H}_4(\text{CH}_3)_2$	135	1 5	4	18				Benzene; toluene (large); mesitylene, durenene, pseudocumene (small)	(43)
$m\text{-C}_6\text{H}_4(\text{CH}_3)_2$	135	24	10				$\text{HCl}$	Toluene	(101)
$m\text{-C}_6\text{H}_4(\text{CH}_3)_2 + \text{CH}_3\text{Cl}$ o- and p- $\text{C}_6\text{H}_4(\text{CH}_3)_2$ + $\text{HCl}$ ....	130-140	8-10	20					Toluene	(127)
$m\text{-C}_6\text{H}_4(\text{CH}_3)_2 + \text{HCl}$	100	6	16 7				No	Mesitylene; pseudocumene; durenene	(66)
$m\text{-C}_6\text{H}_4(\text{CH}_3)_2 + \text{HCl}$	100	6	16 7				No	Benzene; m-xylene (large); mesitylene; pseudocumene	(66)
1,2,4- $\text{C}_6\text{H}_3(\text{CH}_3)_3 \dots$	125-130	2	20					Benzene; toluene; mesitylene; pseudocumene	(3, 4)
1,2,4- $\text{C}_6\text{H}_3(\text{CH}_3)_3 \dots$	150-160	6	7 4				$\text{HCl} + \text{CH}_3\text{Cl}$	Toluene; m-xylene; p-xylene (trace); mesitylene; durenene; isodurene	(87)
1,3,5- $\text{C}_6\text{H}_3(\text{CH}_3)_3 \dots$	150-160	4	9 1				$\text{CH}_3\text{Cl}$	Benzene, 2 per cent; toluene, 8 per cent; m- and p-xylenes, 27 per cent; durenene, 8 per cent; isodurene, 3.2 per cent; mesitylene, 3.6 per cent	(87)
$\text{C}_6\text{H}_4(\text{CH}_3)_4 \dots$	Low		10					Durenene, 5 per cent; isodurene, 16 per cent; m-xylene (large); pseudocumene; benzene, toluene (small amounts)	(47)
1,2,4,5- $\text{C}_6\text{H}_2(\text{CH}_3)_4$ + $\text{HCl} \dots$	130-140		10				$\text{CH}_3\text{Cl}$	Trimethylbenzene; xylene	(87)

\*  $\text{AlBr}_3$ .

TABLE 9—*Concluded*

COMPOUNDS	TEMPERATURES	TIME	CONCENTRATION OF $\text{AlCl}_3$	PRESSURE	PRODUCTS		REFERENCES
					Gases	Liquids and solids	
$\text{C}_6\text{H}(\text{CH}_3)_6$ .....	°C. 50-55	hours 14 days	per cent 33.3	atmospheres		Pentamethylbenzene (large); hexamethylbenzene (small); isodurene; solids	(87)
$\text{C}_6\text{H}(\text{CH}_3)_6 + \text{HCl}$ .....	100-110	4	20	Sealed tube		Hexamethylbenzene; durene; isodurene; solid (m.p. 250°C.)	(87)
$\text{C}_6\text{H}(\text{CH}_3)_6 + \text{HCl}$ .....	130-140		9		Methyl chloride (large)	Lower methylated benzenes	(87)
$\text{C}_6(\text{CH}_3)_6$ .....	Low		9		Gas with more than two carbon atoms	Pentamethylbenzene; tetramethylbenzene; lower methylated benzenes	(47)
$\text{C}_6(\text{CH}_3)_6$ .....	190-200		33.3		Methyl chloride (large)	Pentamethylbenzene (large); durene and isodurene (large); mesitylene; pseudocumene; m-xylene; toluene and benzene (small)	(87)
$\text{C}_6(\text{CH}_3)_6 + \text{HCl}$ .....	264		9.1			Benzene; toluene; complete decomposition of original	(87)

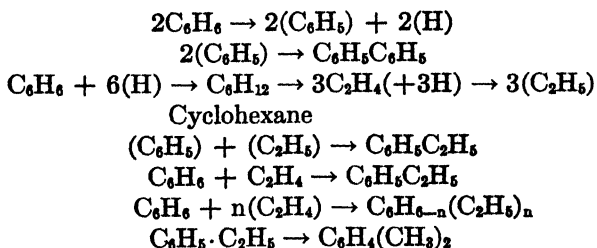
with isoprene in the presence of aluminum chloride, amorphous compounds (6) were formed.

When French turpentine oil and *l*-pinene were treated with aluminum chloride at from 0°C. to room temperature, liquid and solid polymers were produced (130). Reaction at a higher temperature gave a liquid containing paraffins, cycloparaffins, and unsaturated hydrocarbons. French turpentine was also treated for a long period of time with aluminum chloride at room temperature, resulting in the formation of a solid polymer (45). Finnish turpentine oil treated at room temperature yielded a mixture of paraffins, olefins, and cycloparaffins, similar in composition to petroleum. Methyl and ethyl chlorides were also formed (118). Sumatra turpentine, pentane being used as a diluent, polymerized to an oil and resin when subjected to the action of aluminum chloride at -15°C. (141).

#### VIII. BENZENE AND METHYLBENZENES

The reactions of benzene and individual methylbenzenes in the presence of aluminum chloride led to a variable mixture of benzene, methylbenzenes, ethylbenzenes, cycloparaffins, phenylated cycloparaffins, diphenyls, ethylanthracene, and unsaturated compounds. Hydrogen chloride, methyl chloride, and hydrocarbon gases were formed also in some instances. Benzene reacting alone gave alkylated benzenes. The latter, as initial hydrocarbons, reacted to give benzene, lower and higher alkylated benzenes, or diaryl compounds.

Mono- and di-methylbenzene, ethylbenzene, diphenyl, and unsaturated hydrocarbons resulted when benzene was heated above 100°C. with aluminum chloride, as shown in table 9. The formation of these products may be shown by the following equations:



The product, ethylbenzene, arose from the breaking of the benzene ring into two-carbon atom fragments. These two-carbon atom fragments either hydrogenated to an ethyl radical and united with a phenyl radical, or formed an ethylene molecule, which added benzene after scission of a carbon-hydrogen bond in the benzene. Under more strenuous experimental conditions, methyl groups were introduced into the ring. It is probable that the ethyl group splits into methyl and methylene radicals.

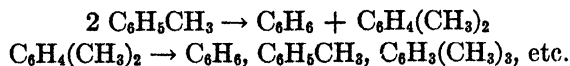


The compounds 1-methyl-3-phenylcyclopentane and diphenylcyclohexane were obtained from benzene in the presence of hydrogen chloride and aluminum chloride (65). The two latter hydrocarbons reacted with benzene to give phenylated cycloparaffins. Phenylcyclohexane and *o*-diphenylcyclohexane as well as diphenyl were present when benzene was kept for three weeks in contact with aluminum bromide (147). These experiments give support to the suggestion that benzene is hydrogenated by the hydrogen produced during the formation of diphenyl. From this mechanism one would expect to find diphenyl as one of the principal reaction products, although actually only small quantities have been reported.

When benzene is heated in the absence of aluminum chloride, diphenyl is the principal product. Alkylated benzenes do not form. In the thermal reactions of benzene, therefore, the carbon-carbon bond (135) in the ring shows great strength, and the principal scission occurs at the carbon-hydrogen linkage. In the presence of aluminum chloride, diphenyl is obtained in smaller amounts than the alkylated benzenes; therefore the carbon-hydrogen bond appears stronger than the carbon-carbon bond, unless, as seems to be the case, alkylation occurs as the result of a preliminary hydrogenation of benzene to cyclohexane, which in turn is dissociated into two-carbon atom fragments.

Phenol and anthracene have been reported frequently as end products in the reaction of benzene in the presence of aluminum chloride. Further, the odor of benzaldehyde was noted, and it was believed that the formation of anthracene resulted from the condensation of two molecules of benzaldehyde. Phenol and its alkyl derivatives have been omitted as products throughout this paper, owing to contamination of the reactants with oxygen.

When the reaction of methylbenzenes with aluminum chloride was carried out at a temperature near the boiling point of the particular compound, the products were either benzene or methylated benzenes. The reactions are given as follows:



These products show that there is a striking difference in the behavior of the benzene ring as one or more methyl groups are attached to it. The point of greatest weakness in the methylbenzenes is the carbon-carbon bond between the ring and side chain. This is another instance where the strength of the bond appears to depend on the side chains.

When toluene was subjected to the aluminum chloride reaction, the principal products were benzene and xylene. It has been reported that higher methylated benzenes are formed (93) and that using a sufficiently

high temperature (47) causes a break in the ring and the formation of ethylated products. When aluminum chloride was not present, benzene was the principal product in the thermal reactions of toluene, while lesser amounts of diphenyl and ditolyl were formed. Apparently, the same relationships in the bond strengths hold, since the higher temperature necessary for the thermal reaction causes the methyl group to pass off in the form of methane or ethane rather than to add to another molecule of toluene.

Upon reaction with aluminum chloride *m*-xylene gave toluene, benzene, and small amounts of tri- and tetra-methylbenzenes. The formation of methyl chloride has also been recorded when 16.7 per cent of aluminum chloride was used (87). When methyl chloride is passed into the reaction mixture (127), only tri- and tetra-methylbenzenes are obtained. The small amounts of the higher methylated benzenes obtained by the other investigators are linked with the loss of the methyl group in the form of methyl chloride. Higher methylated benzenes (3, 4, 66) were obtained at lower temperatures. A detailed study (43) of the concentration of aluminum chloride shows that, in general, the effect of time and the temperature of the reaction seems to overbalance the effect of the concentration of the aluminum chloride. When hydrogen chloride was present in the reaction mixture rather than from its production during the reaction, the tendency for the formation of more highly methylated benzenes was increased.

The tri-, tetra- and penta-methylbenzenes show a greater tendency to form lower, rather than higher, methylated benzenes. This is closely related to the temperature of the reaction, the loss of methyl chloride, and the concentration of the aluminum chloride. The data available are not sufficient to distinguish between these effects.

#### IX. HIGHER ALKYLATED BENZENES

The more highly alkylated benzenes in the presence of aluminum chloride react in the same manner as the methylbenzenes with the difference that propane and isobutane form, depending upon the starting hydrocarbon; that is, the primary scission occurs at the carbon-carbon bond between the ring and the side chain provided that the reaction temperature is not above the boiling point of the alkylated benzene (see table 10). The alkyl group either hydrogenates to give the corresponding paraffin or adds to one of the original alkylated benzenes. The products obtained by experimenters do not show clearly the source of the hydrogen which hydrogenated the alkyl radical; however, formation of the alkylated diaryl compounds would be one source, had they been found when the gaseous paraffin was formed.

TABLE 10  
Reactions of higher alkylated benzenes

COMPOUNDS	TEMPERATURE °C.	TIME hours	CONCENTRATION OF AlCl <sub>3</sub> per cent	PRODUCTS		REFERENCES
				Gases	Liquids and solids	
$C_6H_5C_2H_5$ . . . . .	137		23		Benzene; <i>p</i> - and <i>m</i> -diethylbenzenes (large amount)	(34)
$C_6H_5C_2H_5 + HCl$ . . . . .	136	2			Benzene, 28 per cent; <i>p</i> - and <i>m</i> -diethylbenzenes, 24 per cent; triethylbenzenes, 8 per cent; no xylenes; tar, 5 per cent	(66)
$C_6H_5C_3H_7 + HCl$ . . . . .	100	10			Benzene, 30 per cent; <i>p</i> - and <i>m</i> -diethylbenzenes, 38 per cent; triethylbenzenes, 3 per cent; tar, 2 per cent	(66)
$C_6H_5(n-C_4H_9) + HCl$ . . . . .	100	6	16.7		Benzene, 26 per cent; dipropylbenzenes, 36 per cent; no toluene or xylenes; tar, 2 per cent	(45, 66)
$C_6H_5(iso-C_4H_9)$ . . . . .	100	4	16.7	Propane	Benzene, 34 per cent; <i>m</i> - and <i>p</i> -diisopropylbenzenes, 20 per cent; no toluene or xylenes; tar, 10 per cent	(66)
$C_6H_5(iso-C_4H_9)$ . . . . .	50	6	16.7	Propane (less than at 100°C.)	Benzene, 10 per cent; diisopropylbenzenes, 35 per cent; no toluene or xylenes; tar, 1 per cent	(66)
$C_6H_5(iso-C_5H_{11})$ . . . . .	154	24	10		Benzene, 15 per cent; toluene, 2.7 per cent; xylene, 26.5 per cent	(101)
$C_6H_5(n-C_5H_{11})$ . . . . .	100	5	16.7	No gases	Benzene, 18 per cent; <i>m</i> - and <i>p</i> -dibutylbenzenes, 38 per cent	(66)
$C_6H_5(sec-C_5H_{11})$ . . . . .	140-150	7	20	Gas	Liquid (b.p. 120-210°C.)	(132)
$C_6H_5(tert-C_5H_{11}) + HCl$ . . . . .	80	3	27	Isobutane (42 per cent of theoretical)	Benzene; higher boiling residue	(84)

$C_6H_4(CH_3)(iso-C_3H_7) + HCl$ ...	175					Complex compound $2AlCl_3 \cdot 3C_6H_4$ Toluene; tar (large amount)	(56)
$p-C_6H_4(CH_3)(iso-C_3H_7)$ ...	175	24	25	10		Toluene, 14.3 per cent; benzene, 0.8 per cent; xylene, 7 per cent	(4)
$p-C_6H_4(CH_3)(iso-C_3H_7)$ ...	175	24	25	10		Toluene, 14.3 per cent; benzene, 0.8 per cent; xylene, 7 per cent	(101)
$p-C_6H_4(CH_3)(iso-C_3H_7)$ ...	125-150	2	20	20		Benzene; toluene (small amount)	(124)
$p-C_6H_4(CH_3)(iso-C_3H_7)$ ...	60-98	32-8	20	20		Benzene; toluene; <i>m</i> -xylene; 1-methyl-3,5-diisopropylbenzene; 2,3-dimethylbutane	(124)
$p-C_6H_4(CH_3)(iso-C_3H_7)$ ...	20-35	4	50	50		Benzene; toluene; xylene; 1-methyl-3,5-diisopropylbenzene; high-boiling residue	(92)
$p-C_6H_4(CH_3)(tert-C_4H_9)$ ...	20-35	10	50	50		Toluene; dibutyltoluene; tributyltoluene	(92)
$C_6H_4(C_2H_5)_2 + HCl$ ...	-10					Yellow crystals of $2AlCl_3 \cdot 2C_6H_4(C_2H_5)_2$ HCl	(62, 63)
$p-C_6H_4(n-C_3H_7)_2$ ...	100	2				<i>m</i> -Di- <i>n</i> -propylbenzene, 66.7 per cent; <i>n</i> -propylbenzene; 1,3,5-tripropylbenzene	(9)
$p-C_6H_4(n-C_3H_7)_2$ ...	100	22	33	3		<i>m</i> -Dipropylbenzene, 15.7 per cent; <i>n</i> -propylbenzene, 11.3 per cent	(9)
$m-C_6H_4(n-C_3H_7)_2$ ...	100	22	33	3		<i>m</i> -Di- <i>n</i> -propylbenzene, largely; <i>p</i> -di- <i>n</i> -propylbenzene, small amount	(9)
$1,2,4-C_6H_3(C_2H_5)_3$ ...	100	4				<i>m</i> -Dipropylbenzene, 30 per cent; 1,3,5-tripropylbenzene, 28 per cent; tetrapropylbenzene, 12 per cent	(9)

Ethylbenzene gave benzene and diethylbenzene (3, 4). In the presence of hydrogen chloride, benzene and di- and tri-ethylbenzenes were formed (66), depending on the time and the temperature of the reaction. Xylenes were not formed in these experiments, showing that the ethyl radical was not dissociated. *n*-Propyl- and isopropyl-benzenes gave di-*n*-propylbenzene and diisopropylbenzene, respectively, together with propane and benzene. In the experiments (66) on isopropylbenzene the effect of temperature was shown; at lower temperatures less propane was produced and more diisopropylbenzene formed. At higher temperatures toluene and xylene were obtained, probably resulting from the decomposition of propane or from rupture within the side chain (101).

It was demonstrated that *p*-di-*n*-propylbenzene is rapidly transformed into the meta form at 100°C., while producing some *n*-propylbenzene and ethylbenzenes. The compounds *m*-dipropylbenzene, 1,3,5-tripropylbenzene, and tetrapropylbenzene were formed from 1,2,4-tripropylbenzene.

In the work on butylbenzene (66, 132), butane, benzene, and dibutylbenzene were produced, depending on the temperature of the reaction and the concentration of aluminum chloride.

*p*-Methylisopropylbenzene and *p*-methyl-tertiary-butylbenzene have two different alkyl groups attached to the same ring, and the end products show that the size of the alkyl group has an effect on the nature of the reaction products. At high temperatures and high concentrations of aluminum chloride, propane, benzene, and toluene were obtained from *p*-methylisopropylbenzene, while a lower temperature and concentration of aluminum chloride did not produce propane, but xylene, diisopropylbenzene, and 1-methyl-3,5-diisopropylbenzene were formed. Experiments show that high concentrations of aluminum chloride strip the alkyl groups from the benzene ring, that high temperatures yield toluene, and that low concentrations of aluminum chloride and low temperatures give alkylated benzenes. Similarly, *p*-methyl-tertiary-butylbenzene gave toluene, methyldi-tertiary-butylbenzene, and methyltri-tertiary-butylbenzene. The experiments indicate that isopropyl and tertiary-butyl groups are the first to split from the ring, and that the larger the alkyl group the more readily it breaks off.

#### X. POLYCYCLIC AROMATIC HYDROCARBONS

The data from the experimental work on the reactions of the polycyclic compounds in the presence of aluminum chloride do not lend themselves readily to a study of the mechanism of the reactions. The products formed are more difficult to identify than those from the single ring compounds; consequently accurate, complete, and detailed analyses of the products

have not been obtained in all experiments. Further, these compounds have higher boiling points, which permits a wider range for the reaction temperature and, accordingly, more opportunity for combinations or rearrangements into a larger number of compounds. For polycyclic aromatic compounds, reaction has been effected by either a low temperature and a high concentration of aluminum chloride or the reverse. In general, with these compounds four types of reaction occur: (1) the formation of hydrides of the original compound; (2) the scission of one carbon-hydrogen bond in the original compound and the coupling of the resulting radicals; (3) the breaking-off of one ring giving lower and higher homologues and methylated derivatives; and (4) cyclization by ring closure upon active double bonds. As shown in table 11, naphthalene forms the hydrides of naphthalene, dinaphthyls, tetranaphthyl, methylnaphthalenes, and benzene. Naphthalene and dinaphthyl have been reported to yield perylene. The hydronaphthalenes have lower reaction temperatures than naphthalene, but the same type of reaction products was obtained. This shows that the aromatic ring is more stable than the hydrogenated or partially hydrogenated ring (cycloparaffin or cycloolefin ring).

It was reported that benzene, octahydroanthracene, and octahydrophenanthrene resulted from the action of aluminum chloride on tetralin (91) at 100°C. in accordance with the reaction:



Hydroanthracenes, naphthalene, hydronaphthalene, and methylnaphthalenes have been obtained from anthracene and phenanthrene.

The products from phenylated methanes and ethanes were benzene, dibenzylbenzene, anthracene, and dimethylantracene.

The treatment of 2-methyl-3-phenylethylindene in carbon disulfide solution with aluminum chloride yielded 5,6,6a,11a-tetrahydro-11a-methylchrysofluorene (33), as shown in the equation:

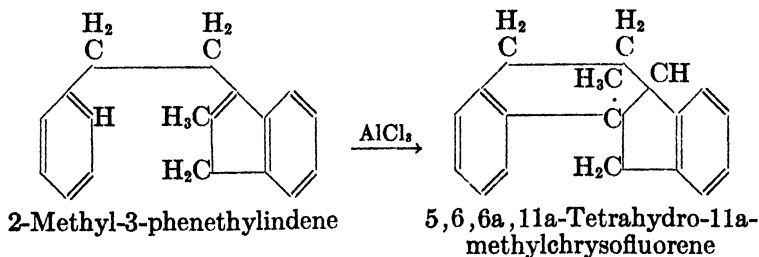


TABLE 11  
Reactions of polycyclic aromatic compounds

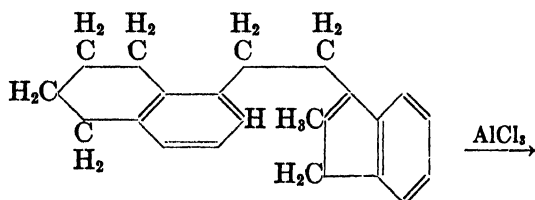
COMPOUNDS	TEMPERATURE °C.	TIME hours	CONCENTRATION OF AlCl <sub>3</sub> per cent	PRODUCTS		REFERENCES
				Gases	Liquids and solids	
Naphthalene .....	100-160	Several	Excess		Benzene; naphthalene hydrides	(46)
Naphthalene .....	100-160	Several	20		Isodinaphthyl; oil	(46)
Naphthalene .....	100-160	Several	25		$\beta, \beta'$ -Dinaphthyl; hydrodinaphthyls	(46)
Naphthalene .....	100	0 5-6 0	50		Tetramethylnaphthalene; C <sub>10</sub> H <sub>12</sub> (tetranaphthyl); C <sub>10</sub> H <sub>12</sub> ; tetramethyldinaphthanthracene, C <sub>18</sub> H <sub>12</sub>	(69)
Naphthalene .....	180	1	80		Perylene	(123)
Tetralin .....	100				Benzene; octracene; octanthrene	(91)
Tetralin .....	30-40		1 0-1.5		Octanthrene; octracene	(125)
Tetralin .....	50-70	10	2		Benzene; octanthrene; octracene; C <sub>14</sub> H <sub>6</sub> ; 1-phenyl-4(2-tetralyl)butane; 2,2'-naphthyl, 2,6'-ditetralyl	(125)
Tetralin .....	70-80	3	4		Octanthrene; dodecahydrotriphenylene; phenylene-bis- and tetralyloctanthrenyl-butane	(125)
Dinaphthyl .....	140	1	80		Perylene	(123)
Hydrodinaphthyl .....					Hydrondinaphthyls	(46)
Anthracene .....	340		3		Carbon; hydroanthracenes; hydronaphthalenes; methylnaphthalene	(108)
Phenanthrene .....	340		4.7	HCl + hydrocarbon gas	Naphthalene; homologs of naphthalene; brown oil	(108)
Phenanthrene + CS <sub>2</sub> .....	100				Powder (believed (C <sub>14</sub> H <sub>10</sub> ) <sub>n</sub> )	(121)
Diphenylmethane .....					Anthracene; benzene	(114)
Diphenylmethane .....	Room	17	66		Oil; benzene; <i>o</i> - and <i>p</i> -dibenzylbenzenes; solid	(122)

	85	17	66	HCl	Same products as at room temperature meso-Dimethylanthracene Trimer of (C <sub>14</sub> H <sub>12</sub> )	(122) (114) (121)
Diphenylmethane						
<i>as</i> -Diphenylethane						
Stilbene + CS <sub>2</sub> ..	100	8	63 7			
<i>as</i> -Diphenylethylene + benzene.....						
<i>cis</i> -Hydrindan ..	100	24	11 9		1,1,3-Triphenyl-3-methylindan, 60 per cent	(15)
2-Methyl-3-phenethylindene + CS <sub>2</sub> .....	0	12	43*		<i>trans</i> -Hydrindan	(153)
1,2,3,4-Tetrahydro-5-( $\beta$ -(2- methyl-3-indenyl)ethyl)- naphthalene + CS <sub>2</sub> .....	0	3	7 7		5,6,6a,11a-Tetrahydro-11a-methylchryso- fluorene, 82 per cent	(33)
7-Isopropyl-4-methyl-3-( $\beta$ -1- naphthylethyl)naphthalene + CS <sub>2</sub> .....	0	3	8 33		1,2,3,4,5,6,6a,11a-Octahydro-11a-methyl- naphtho-(2,1-a)fluorene, 80 per cent	(33)
1,2,3,4-Tetrahydro-5-( $\beta$ -(7- isopropyl-2,4-dimethyl-3- indenyl)ethyl)naphthalene + CS <sub>2</sub> .....	0	4			2,3-Dihydro-4'-isopropyl-7'-methylspiro- (benzonaphthene-1,1'-indan)	(33)
	0	3			1,2,3,4,5,6,6a,11a-Octahydro-10-isopropyl- 7,11a-dimethylnaphtho(2,1-a)fluorene, 75 per cent	(33)
2-Methyl-1-phenethyl-3- $\alpha$ - naphthindene + CS <sub>2</sub> .....	0	4	7		5,6,6a,13a-Tetrahydro-13a-methyldibenzo- ( <i>sg</i> )fluorene, 60 per cent	(28)

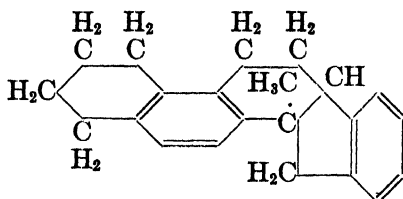
\* AlBr<sub>3</sub> used.



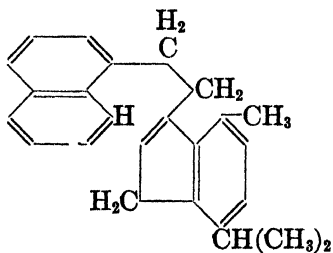
octahydro-11a-methylnaphtho(2,1-a)fluorene, whereas 7-isopropyl-4-methyl-3-( $\beta$ -1-naphthylethyl)indene forms 2,3-dihydro-4'-isopropyl-7'-methylspiro(benzonaphthene-1,1'-indan), and that 1,2,3,4-tetrahydro-5-( $\beta$ -(7-isopropyl-2,4-dimethyl-3-indenyl)ethyl)naphthalene forms 1,2,3,4,5,6,6a,11a-octahydro-10-isopropyl-7,11a-dimethylnaphtho(2,1-a)-fluorene, as follows (33):



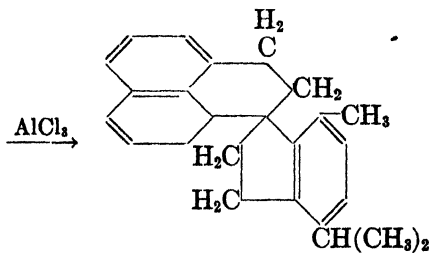
1,2,3,4-Tetrahydro-5-( $\beta$ -(2-methyl-3-indenyl)ethyl)naphthalene; i.e., 3-( $\beta$ -5'-tetralyl-ethyl-2-methylindene



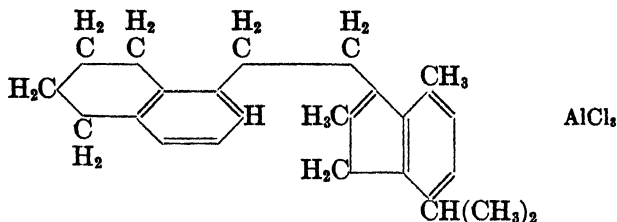
1,2,3,4,5,6a,11a-Octahydro-11a-methylnaphtho(2,1-a)fluorene; i.e., 10-methyl-3,4,10,11,5',6',7',8'-octahydro-2',1'-naphtha-1,2-fluorene



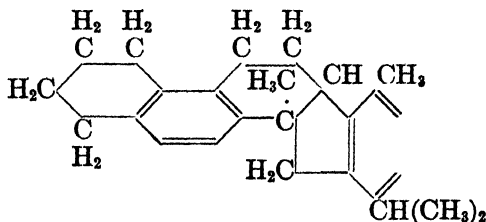
7-Isopropyl-4-methyl-3-( $\beta$ -1-naphthylethyl)indene



2,3-Dihydro-4'-isopropyl-7'-methylspiro(benzonaphthene-1,1'-indan); i.e., 7-methyl-4-isopropylhydrindene-1,7'-spiro-7',8'-dihydrophenalene

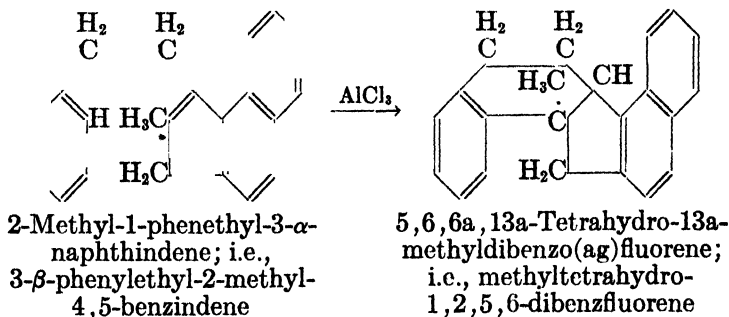


1,2,3,4-Tetrahydro-5-( $\beta$ -(7-isopropyl-2,4-dimethyl-3-indenyl)ethyl)naphthalene; i.e., 3-( $\beta$ -5'-tetralylethyl)-2,4-dimethyl-7-isopropylindene



1,2,3,4,5,6,6a,11a-Octahydro-10-isopropyl-7,11a-dimethylnaphtho(2,1-a)fluorene; i.e., 5,10-dimethyl-8-isopropyl-3,4,10,11,5',6',7',8'-octahydro-2',1'-naphtha-1,2-fluorene

The compound 2-methyl-1-phenethyl-3- $\alpha$ -naphthindene was treated in carbon disulfide solution with aluminum chloride, giving 5,6,6a,13a-tetrahydro-13a-methyldibenzo(ag)fluorene, as follows:



The foregoing five cyclizations are in accordance with the principle of ring closure discussed previously under cycloolefins.

#### XI. AROMATICS WITH OTHER HYDROCARBONS

In addition to the reactions which individual aromatics undergo with aluminum chloride, there are others in which the aromatics react with paraffins, olefins, acetylene, cycloparaffins, cycloolefins, and other aro-

atics, as shown in tables 12 to 17, inclusive. The reactions of aromatics with other hydrocarbons lead to benzene, alkylated and condensed aromatics, arylated paraffins, olefins and cycloparaffins, cycloparaffinic aromatics, and paraffins. The gases formed are propane and butanes.

Because analyses of products were incomplete in many instances, the problem of isomerization has not been dealt with extensively. Many investigators have been satisfied to identify the presence of xylenes, the trimethylbenzenes, etc., without determining the particular isomers; still others merely determined the presence but not the amounts of the differ-

TABLE 12  
*Reactions of aromatics with paraffins*

COMPOUNDS (a)	ADDITIONAL COMPOUNDS (b) (c)	TEMPERATURE	TIME	CONCENTRATION OF $AlCl_3$	RATIO a:b:c	PRODUCTS	REFERENCE
		$^{\circ}C.$	hours	per cent			
$C_6H_6$ . . .	iso- $C_4H_{10}$ + HCl	125	23	10	1:1	Propane, 15 per cent; alkylated benzenes, 25 per cent	(80)
$C_6H_6$ . . . . .	$C_6H_{14}$ + HCl	100	17	10	1:1	Butane, 30 per cent; paraffins below hex- ane, 15 per cent; al- kylated benzenes, 30 per cent (b.p. 90- 200 $^{\circ}C.$ )	(80)
$C_6H_6$ . . . . .	2,2,4-( $CH_3$ ) $_3C_6H_5$ + HCl	25-40	4	5 7	1:0 86	Isobutane; traces of propane and pentane; mono- and di-terti- ary-butylbenzenes; traces of unsaturated compounds	(53)

ent isomers. However, a few observations appear to be sufficiently pronounced to be pointed out. The meta form appears to be the predominant disubstituted form, and the 1,3,5, the trisubstituted form. The latter would follow from the preference for the meta form. It was found that the *o*- and *p*-xylenes gave the meta form, while *m*-xylene was obtained from the 1,2,4- and 1,3,5-trimethylbenzenes (87), and *m*-diethylbenzene was produced from ethylbenzene (3, 4). When substituents differ by more than one methylene group, the above tendencies may not hold. For example, it was found that the above isomerization rules hold for benzene and propene, but not for toluene and propene (16).

TABLE 13  
*Reactions of aromatics with olefins*

COMPOUNDS (a)	ADDITIONAL COMPOUNDS (b) (c)	TEMPERATURE °C.	TIME hours	CONCENTRATION OF AlCl <sub>3</sub> per cent	RATIO a:b:c	PRODUCTS	REFERENCES
C <sub>6</sub> H <sub>6</sub> .....	C <sub>2</sub> H <sub>4</sub>	70-90	Several days	6*	1:7	Mono-, di-, and tri-ethylbenzenes	(10)
C <sub>6</sub> H <sub>6</sub> .....	C <sub>2</sub> H <sub>4</sub>	100	3-4	55*		Mesitylene	(49)
C <sub>6</sub> H <sub>6</sub> .....	C <sub>2</sub> H <sub>4</sub>	70-90	6	16		Mono- to hexa-ethylated benzenes	(99)
C <sub>6</sub> H <sub>6</sub> .....	C <sub>2</sub> H <sub>4</sub> + HCl	70-90	11	7	1:1	Monoeethylbenzene (preferred)	(16)
C <sub>6</sub> H <sub>6</sub> .....	C <sub>2</sub> H <sub>4</sub> + HCl	70-90			1:3	Triethylbenzene (preferred)	(16)
C <sub>6</sub> H <sub>6</sub> .....	C <sub>2</sub> H <sub>4</sub> + HCl	70-75	12-14	11		Di-, tri-, and tetra-ethylbenzenes	(102)
C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub> .....	C <sub>2</sub> H <sub>4</sub> + HCl	70-90	1 3	7		Ethylbenzene; ethyltoluene; higher products	(16)
C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub> .....	C <sub>2</sub> H <sub>4</sub>					<i>sym</i> -Diethyltoluene	(49)
C <sub>6</sub> H <sub>4</sub> (CH <sub>3</sub> ) <sub>2</sub> .....	C <sub>2</sub> H <sub>4</sub>		1 5	5*		<i>sym</i> -Ethylxylene	(49)
C <sub>10</sub> H <sub>8</sub> (naphthalene) ..	C <sub>2</sub> H <sub>4</sub>	240	80-85	5 3*		Mono- and di-ethylnaphthalenes	(150)
C <sub>6</sub> H <sub>6</sub> .....	C <sub>2</sub> H <sub>4</sub> + HCl	70	12	7		Mono- to hexa-isopropylated benzenes	(16)
C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub> .....	C <sub>2</sub> H <sub>4</sub> + HCl	70-90	1 3	7		<i>p</i> -Cymene; benzene; toluene; xylene; triethylbenzene; <i>m</i> -cymene (small)	(16)
C <sub>10</sub> H <sub>8</sub> (naphthalene) ..	C <sub>2</sub> H <sub>4</sub> + C <sub>2</sub> H <sub>14</sub> (hexahydro- toluene)	80		1.3	1:1.2	Diisopropylnaphthalene; less mono- and tetra-isopropylbenzenes	(74)
C <sub>10</sub> H <sub>8</sub> .....	C <sub>2</sub> H <sub>4</sub> + C <sub>2</sub> H <sub>12</sub> (hexahydro- benzene)	20		0.8	1:1.8:8	Tetrabutyl-naphthalene	(74)
C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub> .....	C <sub>2</sub> H <sub>10</sub>	25-30		3.3	2:5	Amyltoluene	(42)

\* Calculated with C<sub>2</sub>H<sub>4</sub>.

TABLE 14  
*Reactions of aromatics with acetylene*

COMPOUNDS (a)	ADDITIONAL COMPOUNDS (b) (c)	TEMPERATURE °C.	TIME hours	CONCENTRATION OF $\text{AlCl}_3$ per cent	RATIO a. b. c	PRODUCTS	REFERENCES
$\text{C}_6\text{H}_6$ ..	$\text{C}_2\text{H}_2$	20	5	10	16:1	Diphenylalkanes; polymers	(21)
$\text{C}_6\text{H}_6$ ..	$\text{C}_2\text{H}_2$	Room	50	20*	10:1	Styrene, 80 per cent; <i>as</i> -diphenylethane, 15 per cent; diphenyl, 5 per cent	(139)
$\text{C}_6\text{H}_6$ ..	$\text{C}_2\text{H}_2$	Room	Several days			Ethylbenzene; diphenyl; styrene	(109)
$\text{C}_6\text{H}_6$ ..	$\text{C}_2\text{H}_2$	70-80	3	18		<i>as</i> -Diphenylethane; 9, 10-dimethylanthracene hydride	(27)
$\text{C}_6\text{H}_5\text{CH}_3$ ..	$\text{C}_2\text{H}_2$	70-80	3	18		Xylene; mesitylene; pseudocumene; <i>p</i> , <i>p'</i> -tolylethane; 2, 7-dimethylanthracene; $\beta$ -methylanthracene; 1, 6-dimethylanthracene	(27)

\* Calculated with  $\text{C}_2\text{H}_2$ .TABLE 15  
*Reactions of aromatics with cycloparaffins*

COMPOUNDS	ADDITIONAL COMPOUNDS (b) (c)	TEMPERATURE °C.	TIME hours	CONCENTRATION OF $\text{AlCl}_3$ per cent	PRODUCTS	REFERENCES
$\text{C}_6\text{H}_6$ ..	Cyclopropane + HCl	Room			Propylbenzene; hexapropylbenzene	(54)
$\text{C}_6\text{H}_5(\text{iso-C}_3\text{H}_7)$	Cyclohexane + HCl	80	3	11 9	Propane, 33 per cent; phenylcyclohexane; methylcyclopentane; benzene; <i>p</i> -diisopropylbenzene	(84)
$\text{C}_6\text{H}_5(\text{sec-C}_4\text{H}_9)$ ..	Cyclohexane + HCl	80	3	11 4	<i>n</i> -Butane, 35 per cent	(84)
$\text{C}_6\text{H}_5(\text{tert-C}_4\text{H}_9)$ ..	Cyclohexane + HCl	70	1	11.4	Isobutane, 61 per cent	(84)
$\text{C}_6\text{H}_5(\text{tert-C}_4\text{H}_{11})$ ..	Cyclohexane + HCl	65-82	2	15 5	Isopentane, 60 per cent	(84)
$\text{C}_6\text{H}_5(\text{iso-C}_3\text{H}_7)$ ..	Decahydronaphthalene + HCl	80	3	13 3	Propane, 53 per cent	(84)
$\text{C}_6\text{H}_5(\text{sec-C}_4\text{H}_9)$ ..	Decahydronaphthalene + HCl	80	3	12 8	<i>n</i> -Butane, 71 per cent	(84)
$\text{C}_6\text{H}_5(\text{tert-C}_4\text{H}_9)$ ..	Decahydronaphthalene + HCl	60-78	1 25	12 8	Isobutane, 94 per cent; benzene; decahydronaphthylbenzene	(84)

TABLE 16  
Reactions of aromatics with cycloolefins

COMPOUNDS (a)	ADDITIONAL COMPOUNDS (b) (c)	TEMPERATURE	TIME	CONCENTRATION OF $\text{AlCl}_3$	RATIO a b c	PRODUCTS	REFERENCE
$\text{C}_6\text{H}_6$ . . . . .	$\text{C}_6\text{H}_{10}$ (cyclohexene)	Room	3 hours	per cent 10	4:1	Cyclohexylbenzene, 70 per cent; 1,2-diphenylcyclohexane	(18)
$\text{C}_6\text{H}_6$ . . . . .	$\text{C}_6\text{H}_{10} + \text{HCl}$	55	5	9	1:1	Cyclohexylbenzene; high-boiling residue	(16)
$\text{C}_6\text{H}_5\text{CH}_3$ . . . . .	$\text{C}_6\text{H}_{10} + \text{CS}_2$	Room	3	5-6	4:1	<i>o</i> - and <i>p</i> -Cyclohexyltoluenes, 63 per cent	(18)
<i>m</i> - $\text{C}_6\text{H}_4(\text{CH}_3)_2$ . . . . .	$\text{C}_6\text{H}_{10} + \text{CS}_2$	Room	3	5-6	4:1	5-Cyclohexyl-1,3-dimethylbenzene, 35 per cent	(18)
<i>p</i> - $\text{C}_6\text{H}_4(\text{CH}_3)_2$ . . . . .	$\text{C}_6\text{H}_{10} + \text{CS}_2$	Room	3	5-6	4:1	2-Cyclohexyl-1,4-dimethylbenzene, 45 per cent; 1,4-dicyclohexyldimethylbenzene (small)	(18)
<i>sym</i> - $\text{C}_6\text{H}_3(\text{CH}_3)_3$ . . . . .	$\text{C}_6\text{H}_{10} + \text{CS}_2$	Room	3	4 2	5:1:5	2-Cyclohexyl-1,3,5-trimethylbenzene	(18)
<i>p</i> - $\text{C}_6\text{H}_4(\text{CH}_3)(\text{iso-C}_3\text{H}_7)$ . . . . .	$\text{C}_6\text{H}_{10} + \text{CS}_2$	Room	3	3	6:1:6	Cyclohexylisopropyl-1-methyl-4-benzene, 40 per cent; dicyclohexylisopropyl-1-methyl-4-benzene	(18)
$\text{C}_{10}\text{H}_8$ . . . . .	$\text{C}_6\text{H}_{10} + \text{CS}_2$	Room	3	4 4	1:2:1	Cyclohexylnaphthalene; dicyclohexylnaphthalene	(18)
$\text{C}_{10}\text{H}_{12}$ (tetralin)	$\text{C}_6\text{H}_{10} + \text{CS}_2$	Room	0 66	4.4	1:2:1	Cyclohexyltetralin	(18)
$(\text{C}_6\text{H}_5)_2\text{CH}_2$ . . . . .	$\text{C}_6\text{H}_{10} + \text{CS}_2$	Room	3	4 3	1:2:1	<i>p</i> -Cyclohexyldiphenylmethane; <i>p</i> -benzyl-diphenyl	(18)
$\text{C}_6\text{H}_4$ . . . . .	$\text{C}_6\text{H}_9\text{CH}_3$	Room	3	10	1:3:5	Dimethyldicyclohexylbenzene; methylcyclohexylbenzene	(18)
$(\text{C}_6\text{H}_5)_2\text{CH}_2$ . . . . .	$\text{C}_6\text{H}_9\text{CH}_3 + \text{CS}_2$	Room	3	4 3	1:0 4:1	<i>p</i> -Methylcyclohexyldiphenylmethane	(18)
$\text{C}_6\text{H}_6$ . . . . .	Menthene	Room	3	12	2:1	Menthylbenzene	(18)

TABLE 17  
Reactions of aromatics with aromatics

COMPOUNDS (a)	ADDITIONAL COMPOUNDS (b) (c)	TEMPER- ATURE	TIME	CONCENTRATION OF AlCl <sub>3</sub>	RATIO a:b:c	PRODUCTS	YIELD- PERCENT
			hours	per cent			
<i>m</i> - or <i>p</i> -C <sub>6</sub> H <sub>4</sub> (CH <sub>3</sub> ) <sub>2</sub> ..	C <sub>6</sub> H <sub>6</sub>	100	6	0.9-0.5	10:1	Toluene	(20)
C <sub>6</sub> H <sub>5</sub> (C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> ..	C <sub>6</sub> H <sub>6</sub>	100	6	2	10:1	Ethylbenzene; residue	(20)
C <sub>6</sub> H <sub>4</sub> (C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> + C <sub>6</sub> H <sub>5</sub> (C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> ..	C <sub>6</sub> H <sub>6</sub>	150-200	6	2	8:1	Ethylbenzene; residue	(20)
C <sub>6</sub> H <sub>5</sub> - <sub>3</sub> (iso-C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> ..	C <sub>6</sub> H <sub>6</sub>	100	6	0.65	10:1	Isopropylbenzene; residue	(20)
C <sub>6</sub> H <sub>5</sub> ( <i>tert</i> -C <sub>4</sub> H <sub>9</sub> ) ..	C <sub>6</sub> H <sub>5</sub> C <sub>2</sub> H <sub>5</sub> + HCl	80	3	30	1:1	Isobutane, 75 per cent; diphenyl-ethylbenzene; higher boiling residues	(85)
C <sub>6</sub> H <sub>5</sub> ( <i>tert</i> -C <sub>4</sub> H <sub>9</sub> ) ..	C <sub>6</sub> H <sub>6</sub> + HCl	85	3	30	2:3	Isobutane, 61 per cent; higher boiling residues	(85)
C <sub>6</sub> H <sub>5</sub> - <sub>3</sub> ( <i>tert</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>3</sub> ..	C <sub>6</sub> H <sub>6</sub>	100	6	2	10:1	<i>tert</i> -Butylbenzene; residue	(20)
C <sub>6</sub> H <sub>5</sub> - <sub>3</sub> ( <i>tert</i> -C <sub>4</sub> H <sub>9</sub> ) <sub>3</sub> ..	C <sub>6</sub> H <sub>6</sub>	100	6	0.9	10:1	<i>tert</i> -Amylbenzene; residue	(20)
<i>p</i> -(C <sub>6</sub> H <sub>4</sub> )(CH <sub>3</sub> )(iso-C <sub>2</sub> H <sub>5</sub> ) ..	C <sub>6</sub> H <sub>6</sub>	100	10-6	2.5-0.4	10:1-1.5	Toluene; isopropylbenzene; residue	(20)
C <sub>12</sub> H <sub>10</sub> (phenanthrene) ..	C <sub>6</sub> H <sub>6</sub>	80	1	14.5	1:0.14	2,3,10,11-Dibenzoperylene	(26)
C <sub>10</sub> H <sub>8</sub> ..	C <sub>6</sub> H <sub>5</sub> C <sub>2</sub> H <sub>5</sub>	80	5	5.0	1:1	Diethylbenzene; benzene; diethyl-naphthalene; higher products	(99)
C <sub>10</sub> H <sub>8</sub> ..	C <sub>6</sub> H <sub>4</sub> (iso-C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> + HCl	90	4.5		1:0.48	Isopropyl-naphthalene, 4.3 per cent; higher boiling products	(16)
C <sub>6</sub> H <sub>5</sub> C≡CC <sub>6</sub> H <sub>5</sub> ..	C <sub>6</sub> H <sub>6</sub> + HCl	Room	6	0.9	1:123	<i>sym</i> -Tetraphenylethane, 64 per cent	(1)
C <sub>6</sub> H <sub>5</sub> C≡CC <sub>6</sub> H <sub>5</sub> ..	C <sub>6</sub> H <sub>6</sub> + HCl	Room	20	8	1:103	Dibenzyl, 32 per cent	(1)
C <sub>6</sub> H <sub>5</sub> CH=CHC <sub>6</sub> H <sub>5</sub> ..	C <sub>6</sub> H <sub>6</sub> + HCl	Room	54			Dibenzyl, 20 per cent	(2)

$C_6H_5CH=CHC_6H_5$ . . . . .	$C_6H_6 + HCl$	Room	8	1.4	1:31	1,1,2-Triphenylethane, 49 per cent	(1)
$C_6H_5CH=C(C_6H_5)_2$ . . . . .	$C_6H_6 + HCl$	Room	20	0.71	1:89	s-Tetraphenylethane, 70 per cent	(1)
$C_6H_5CH=C(C_6H_5)_2$ . . . . .	$C_6H_6 + HCl$	Room				Dibenzyl, 28 per cent	(1)
$(C_6H_5)_2C=C(C_6H_5)_2$ . . . . .	$C_6H_6 + HCl$	Room		12.3	1:82	Dibenzyl	(1)
$(C_6H_5)_2C=C(C_6H_5)_2$ . . . . .	$C_6H_6$	Room	3 days	4.55	1:85	9,10-Diphenylphenanthrene, 25 per cent; diphenylmethane	(17)
$C_6H_5CH_2-CH(C_6H_5)_2$ . . . . .	$C_6H_6 + HCl$	Room				Dibenzyl, 57 per cent	(1)
$(C_6H_5)_2CH-CH(C_6H_5)_2$ . . . . .	$C_6H_6 + HCl$	Room				Dibenzyl, 54 per cent	(1)

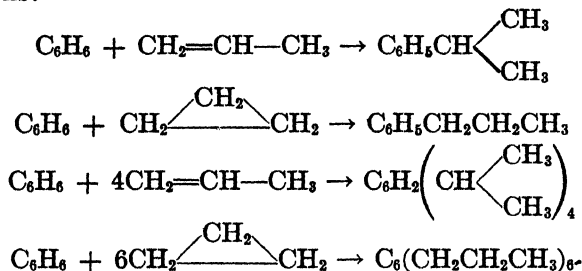


Benzene reacts with isopentane and hexane in the presence of aluminum chloride and hydrogen chloride to form ethylbenzene (76a). The data show that isopentane is probably decomposed initially into ethylene and propane, whereas hexane forms ethylene and isobutane, and that ethylene alkylates the benzene. In the reaction between benzene and ethylene, one molecule of aluminum chloride causes over 100 molecules of ethylene to react with benzene to form ethylbenzene. The rate of stirring of the reaction mixture is equivalent to increasing the contact surface in heterogeneous systems and is an important factor in the rate of ethylation, as is the concentration of aluminum chloride (16, 99).

Benzene and alkylated benzenes gave propylbenzenes in the presence of propene, but the reaction proceeded less rapidly than with ethylene.

There is some doubt as to the exact nature of the reaction products with acetylene, since workers have not checked their results, reporting *as*-diphenylethane, diphenyl, and styrene as reaction products. Toluene, in the presence of acetylene, formed alkylated anthracenes.

Cyclopropane reacts readily at room temperature with benzene in the presence of aluminum chloride and hydrogen chloride to give from mono- to hexa-propylbenzenes (54). This reaction is similar to that between benzene and propene (16). The following equations indicate the analogous reactions:



Cyclohexane reacts readily at 65° to 80°C. with isopropylbenzene, secondary-butylbenzene, tertiary-butylbenzene, and tertiary-amylbenzene in the presence of aluminum chloride and hydrogen chloride to dealkylate the benzenes and yield the corresponding paraffin, namely, propane, *n*-butane, isobutane, and isopentane (84). Substitution of decahydronaphthalene for cyclohexane as a hydrogen donor gave improved yields of paraffins. The source of the hydrogen necessary to reduce the alkyl group to paraffin was indicated by the isolation of phenylcyclohexane and decahydronaphthylbenzene, as in the following examples:

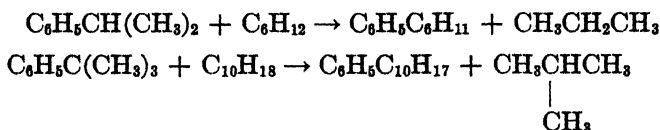


TABLE 18  
Aluminum chloride addition compounds

FORMULA OF COMPLEX	CHARACTERISTIC PROPERTIES		REFERENCES
	Color and physical state	Stability	
$\text{AlCl}_3 \cdot 2\text{C}_2\text{H}_5 \cdot 2\text{H}_2\text{O}$ .....	Colorless crystals	Unstable	(57)
$\text{AlCl}_3 \cdot 3\text{C}_2\text{H}_5 \cdot \text{H}_2\text{O}$ .....	Colorless crystals	Unstable	(58, 60, 61, 62)
$2\text{AlCl}_3 \cdot \text{C}_6\text{H}_{10}$ .....		Stable	(60, 61)
$2\text{AlCl}_3 \cdot \text{C}_6\text{H}_{10} \cdot 6\text{C}_6\text{H}_6$ .....	Fuming liquid	Unstable	(55, 59)
$\text{AlCl}_3 \cdot 3\text{C}_6\text{H}_6$ .....	Fuming liquid	Very unstable	(55, 59, 60)
$\text{AlCl}_3 \cdot 3\text{C}_6\text{H}_5\text{CH}_3$ .....		Stable	(60)
$2\text{AlCl}_3 \cdot \text{C}_6\text{H}_5(\text{CH}_3)_2$ .....			(60)
$2\text{AlCl}_3 \cdot \text{C}_6\text{H}_5(\text{CH}_3)_2 \cdot 6\text{C}_6\text{H}_6$ .....			(60)
$2\text{AlCl}_3 \cdot \text{C}_6\text{H}_5(\text{CH}_3)_2 \cdot 5\text{C}_6\text{H}_5\text{CH}_3$ .....			(60)
$2\text{AlCl}_3 \cdot 5\text{C}_6\text{H}_5(\text{CH}_3)_2$ .....			(60)
$2\text{AlCl}_3 \cdot \text{C}_6\text{H}_5(\text{CH}_3)_2 \cdot 3\text{C}_6\text{H}_5(\text{CH}_3)_2$ ..			(56)
$2\text{AlCl}_3 \cdot 3\text{C}_6\text{H}_5(\text{CH}_3)_2 (\text{CHMe}_2)_2$ ..	Heavy liquid	Stable	(60, 61, 62)
$2\text{AlCl}_3 \cdot \text{C}_6\text{H}_5(\text{C}_2\text{H}_5)_2$ .....	Liquid		(63)
$2\text{AlCl}_3 \cdot \text{C}_6\text{H}_5(\text{C}_2\text{H}_5)_2 \cdot \text{C}_6\text{H}_6$ .....			(60, 61)
$2\text{AlCl}_3 \cdot \text{C}_6\text{H}_5(\text{C}_2\text{H}_5)_2 \cdot 5\text{C}_6\text{H}_5\text{CH}_3$ .....			(60, 61)
$2\text{AlCl}_3 \cdot \text{C}_6\text{H}_5(\text{C}_2\text{H}_5)_2 \cdot 4\text{C}_6\text{H}_5(\text{CH}_3)_2$ ..			(61)
$2\text{AlCl}_3 \cdot \text{C}_6\text{H}_5(\text{C}_2\text{H}_5)_2 \cdot 4\text{C}_6\text{H}_5\text{C}_6\text{H}_5$ .....			(60)
$2\text{AlCl}_3 \cdot \text{C}_6\text{H}_5(\text{C}_2\text{H}_5)_2 \cdot 3\text{C}_6\text{H}_5(\text{CH}_3)_2$ ..			(60, 61)
$2\text{AlCl}_3 \cdot \text{C}_6\text{H}_5(\text{C}_2\text{H}_5)_2 \cdot 3\text{C}_6\text{H}_5\text{C}_6\text{H}_7$ .....			(60)
$2\text{AlCl}_3 \cdot \text{C}_6\text{H}_5(\text{C}_2\text{H}_5)_2 \cdot \text{C}_6\text{H}_5(\text{CHMe}_2)_2 \cdot \text{HCl}$	Yellow crystals	Unstable	(63)
$\text{AlCl}_3 \cdot \text{C}_6\text{H}_5(\text{C}_2\text{H}_5)_2$ .....			(60, 61)
$2\text{AlCl}_3 \cdot 2\text{C}_6\text{H}_5(\text{C}_2\text{H}_5)_2 \cdot \text{HCl}$ .....	Yellow crystals	Unstable	(62, 63)
$2\text{AlCl}_3 \cdot \text{C}_6\text{H}_5(\text{C}_2\text{H}_5)_2 \cdot 3\text{C}_6\text{H}_5(\text{C}_2\text{H}_5)_2$ .....			(60)
$2\text{AlCl}_3 \cdot \text{C}_6\text{H}_5(\text{CHMe}_2)_2$ .....			(62, 63)
$2\text{AlCl}_3 \cdot \text{C}_6\text{H}_5(\text{CHMe}_2)_2 \cdot \text{C}_6\text{H}_6$ .....	Green liquid	Unstable	(62, 63)
$2\text{AlCl}_3 \cdot \text{C}_6\text{H}_5(\text{CHMe}_2)_2 \cdot 6\text{C}_6\text{H}_6$ .....	Liquid		(62, 63)
$2\text{AlCl}_3 \cdot 2\text{C}_6\text{H}_5(\text{CHMe}_2)_2 \cdot \text{HCl}$ ..	Yellow crystals	Unstable	(62, 63)
$2\text{AlCl}_3 \cdot 2\text{C}_6\text{H}_5(\text{CMe}_2)_2 \cdot \text{HCl}$ .....	Yellow crystals	Unstable	(62)
$2\text{AlBr}_3 \cdot \text{C}_6(\text{C}_2\text{H}_5)_6$ .....	Colorless crystals		(83)

Toluene and ethylbenzene did not undergo reactions similar to those just given, indicating stability of the bond between phenyl and both methyl and ethyl groups.

When benzene and cyclohexene reacted in the presence of aluminum chloride and carbon disulfide, it was indicated that the cyclohexyl radical formed added to the benzene ring; when several groups were present, the 1,3,5-position was the preferred one (18, 19). The carbon disulfide used as solvent did not appear to change the nature of the reaction. The phenylmethanes with cyclohexene formed the cyclohexylphenylmethanes. Menthene and benzene formed menthylbenzene.

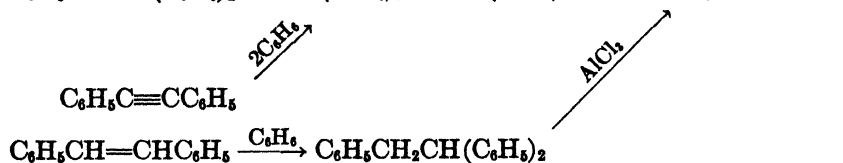
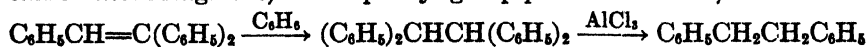
TABLE 19  
*Hydrocarbon group reactions with aluminum chloride*

	PARAF- FINS	OLEFINS	ACETYL- ENES	CYCLO- PARAF- FINS	CYCLO- OLEFINS	TER- PENES	ARO- MATIC
<b>A. Reactions:</b>							
1. Dissociation .....	+	+	-	+	-	+	+
2. Dehydrogenation.....	-	+	-	+	+	+	+
3. Alkylation .....	+	+	+	+	-	-	+
4. Isomerization.....	+	+	-	+	+	-	+
5. Cyclization.....	-	+	+	-	+	-	+
6. Polymerization.....	-	+	+	-	+	+	+
7. Hydrogenation.....	-	+	-	-	+	+	+
8. Addition compounds with $AlCl_3$ .....	-	+	+	-	-	-	+
<b>B. Products formed:</b>							
1. Paraffins.....							
2a. Butanes.....	+	+	-	+	-	-	+
b. Higher and lower.....	+	+	-	+	-	+	+
3. Olefins (unsaturates).....	+	+	+	+	-	+	+
4. Cycloparaffins.....	+	+	-	+	+	+	+
5. Aromatics .....	-	+	-	+	+	+	+
6. Carbon.....	+	+	-	-	-	-	+
7. Liquids of unknown constitu- tion .....	+	+	+	+	-	+	+
8. Chlorinated compounds.....	+	+	-	+	-	+	+

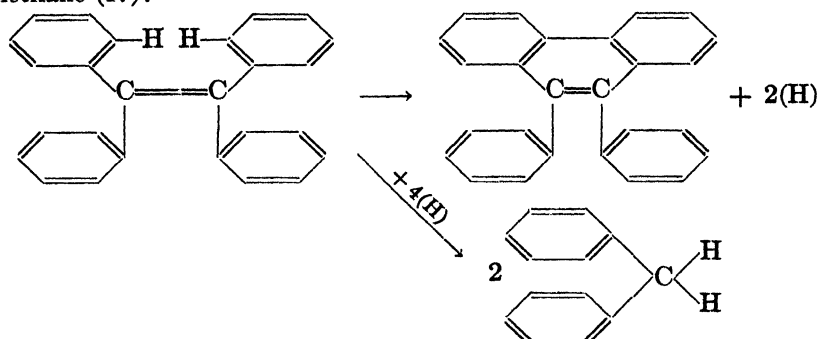
Alkylated benzenes in the presence of benzene redistributed the alkyl groups so that only one alkyl group remained on each benzene ring. From this, it appears that monosubstituted benzene is the most stable. In all redistributions of ethyl groups, it is interesting to note that the ethyl group did not change to a higher or lower alkyl radical. Ethylbenzene was found to act as hydrogen donor in the scission of tertiary-butylbenzene (85). It has been suggested (84) that important applications of similar hydrogen donor reactions are to be found in determining the structure of

alkyl groups attached to an aromatic nucleus, and the relative stability of bonds in hydrocarbons.

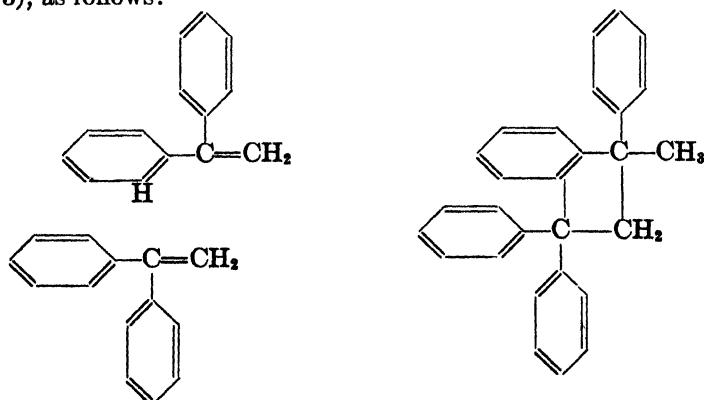
Polyarylated acetylenes, ethylenes, and ethanes formed dibenzyl, as a result of the action of benzene and aluminum chloride. This indicates a redistribution of phenyl groups so that two phenyls remain on each two-carbon atom fragment, or one phenyl group per carbon atom, as follows:



Tetraphenylethylene upon refluxing with benzene and aluminum chloride dehydrogenated to form 9,10-diphenylphenanthrene and diphenylmethane (17):



The compound *as*-diphenylethylene upon prolonged contact with aluminum chloride in the presence of benzene polymerized to a saturated dimer, to which was ascribed the structure of 1,1,3-triphenyl-3-methylindan (15), as follows:



It was thought desirable to tabulate, as far as possible, the reactions which occur to the greatest extent in the case of the hydrocarbon groups studied. The plus signs in table 19 indicate that the hydrocarbons dissociate, dehydrogenate, hydrogenate, isomerize, cyclicize, polymerize, alkylate, and form addition compounds, or undergo a combination of some of these reactions. The detailed data are given in the preceding tables.

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# THE CHEMISTRY OF THE ALKALI AMIDES. II

F. W. BERGSTROM

*Department of Chemistry, Stanford University, California*

AND

W. CONARD FERNELIUS

*Department of Chemistry, The Ohio State University, Columbus, Ohio*

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## PART I. PREPARATION, STORAGE, AND INORGANIC REACTIONS

### I. INTRODUCTION

The rapid rise in the use of the alkali amides in industry and in the synthetic organic laboratory, as well as the scientific interest attendant upon these compounds, prompted a few years ago the preparation of a complete review of the literature bearing on this topic (14). Since that time (1932) activity in this field has continued, and several important papers have appeared. Also it is now evident that some omissions of past work were made in the original review. Hence it seems desirable to supplement the former by making the necessary additions and by bringing it up to date. The same organization of data will be followed in the supplement so that cross reference may be readily accomplished.

## II. HISTORICAL

Wöhler (90) states that both Berzelius (16) and Gmelin (37), on the basis of the results of Gay-Lussac and Thénard (35), showed that the alkali amides had the formula  $MNH_2$ . One gathers the impression from Wöhler's paper that these demonstrations were made before Gay-Lussac and Thénard were certain in their own minds of the true formula of these compounds. The question was important to Wöhler because he had just prepared certain amide compounds of tungsten.

## III. THE ALKALI AMIDES AS THE CAUSTIC ALKALIS OF THE AMMONIA SYSTEM

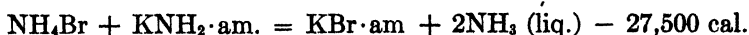
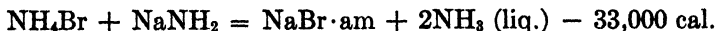
*Action on indicators; neutralization reactions*

Fredenhagen (34) has discussed the behavior of indicators toward liquid ammonia solutions of potassium amide and has found the potential of the following cell,

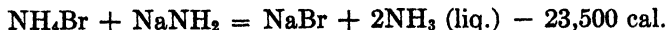


to be 0.746 volt.

By means of a liquid ammonia calorimeter, Kraus and Ridderhof (59) have determined the energies at  $-33.4^\circ C.$  of the reactions represented by the following equations:



Introducing the energy change accompanying the solution of sodium bromide in liquid ammonia ( $-9500 \text{ cal.}$ ) into the first equation, one obtains the energy equation,



from which one computes the heat of formation of liquid ammonia at  $-33.4^\circ C.$  to be  $17,000 \text{ cal.}$  Similarly one obtains the equation,



which shows that the heat of neutralization of an ammono acid by an ammono base in liquid ammonia is much larger than the heat of neutralization of strong acids and bases in water.

*Precipitation of insoluble bases*

The interaction of potassium amide and barium bromide produces barium amide (47). Liquid ammonia solutions of zirconium bromide

and potassium amide (not in excess) produce an equimolecular mixture of  $\text{Zr}(\text{NH})_2$  and  $\text{Zr}(\text{NH})\text{NK}$  (96).

#### *Amphoteric amides*

In addition to the salts of amphoteric amides listed previously (14, p. 51), the following have been prepared: a stannate,  $\text{Sn}(\text{NK})_2 \cdot 4\text{NH}_3$  (11, 31); a stannite,  $\text{SnNK} \cdot 2\text{NH}_3$  (9); a titanate,  $\text{NTiNHK}$  (77); two zirconates,  $\text{Zr}(\text{NK})_2\text{NH}_3$  and  $\text{Zr}(\text{NH})\text{NK}$ ; and two thorates,  $\text{Th}(\text{NK})_2 \cdot \text{KNH}_2$  and  $\text{Th}(\text{NH})\text{NK} \cdot \text{NH}_3$  (96).

#### IV. PREPARATION OF THE ALKALI AMIDES

In preparing sodium amide by the interaction of molten sodium and gaseous ammonia, it is essential that the containing vessel be constructed of a material which is not attacked by the molten amide (14, pp. 54-5). Copper vessels have been found to be satisfactory for the preparation of sodium amide (78). The preparation, manipulation, and storage of sodium amide recently has been described in some detail (36). Certain substances, notably sodium hydroxide (78), sodium oxide, and the metals, alloys, oxides, and oxygen salts of the chromium and adjacent groups of metals, exert a catalytic effect upon the reaction between molten sodium and gaseous ammonia (103, 107). Such catalysts are used to facilitate the manufacture of sodium amide in large quantities.

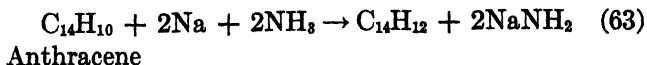
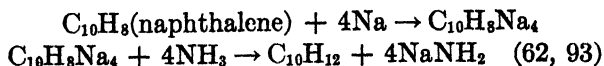
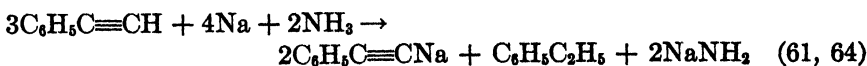
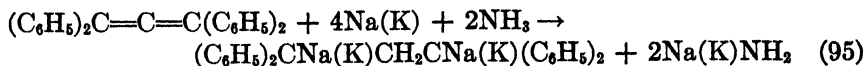
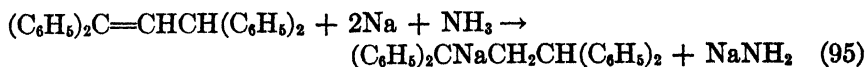
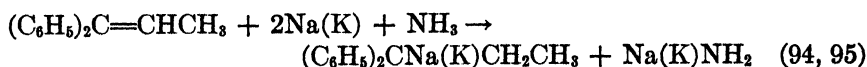
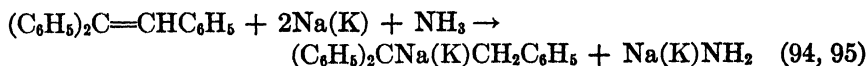
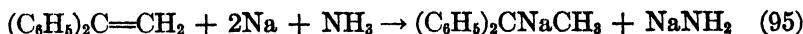
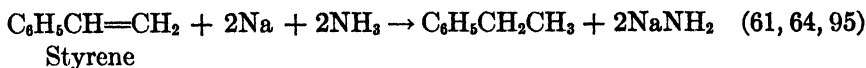
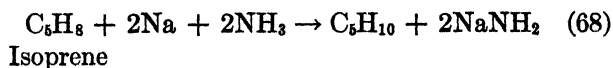
The reaction between liquid ammonia and dissolved alkali metals is very susceptible to catalytic effects (14, pp. 58-9). For the rapid preparation of sodium amide, Vaughn, Vogt, and Nieuwland (82) recommend the use of ammonia-soluble iron (cf. 105), nickel, or cobalt salts (usually the nitrates, which are reduced to the free metals by the sodium) in the presence of sodium oxides. Iron is approximately 40 per cent more efficient than nickel and 20 per cent more than cobalt, while sodium hydroxide is a pronounced, though weak, negative catalyst. Calcium amide could not be prepared by the above procedure, although finely divided silver is an effective catalyst (19). Burgess and Smoker (18; cf. 7) have pointed out the catalytic effect of metallic manganese on the reaction between liquid ammonia and dissolved sodium. Magnesium (6, 10), aluminum (6, 8), beryllium (12), and silver (19) act as catalysts for the interaction of liquid ammonia and dissolved sodium and potassium metals, although the catalytic activity of some metals in the compact form appears to be very low (99, 106). Ferric oxide has been much used as a catalyst for the preparation of potassium amide. Bergstrom (13) has shown that this oxide is a more effective catalyst for the above reaction than either metallic iron or platinum. Ignited cobalt oxide ( $\text{Co}_3\text{O}_4$ ) is also an excellent catalyst for the potassium-ammonia reaction. The

use of these oxides as catalysts is not to be recommended for producing an amide of highest purity, because of interaction between the oxides and potassium amide.

During the last few years the possibility of preparing sodium amide by the electrolysis of a liquid ammonia solution of sodium chloride has been investigated in some detail (1, 3, 83, 98). Sodium amide is obtained similarly in the electrolysis of sodium nitrate (2) and sodium nitrite (4).

The alkali amides are frequently formed as products of the reducing action of the alkali metals on organic compounds in liquid ammonia (56). The following examples illustrate this type of reaction (cf. 24, 30, 92):

### *Hydrocarbons*

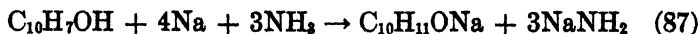


### *Halides*

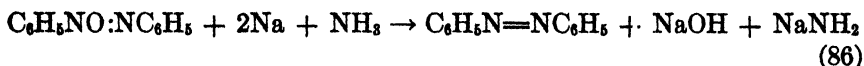
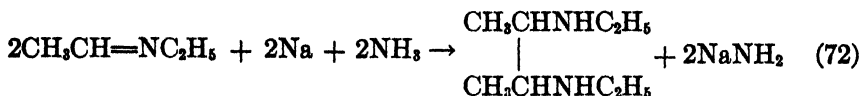


$\text{NaNH}_2$  is formed during the similar reduction of certain paraffin polyhalides (21, 22, 23).

*Naphthols*



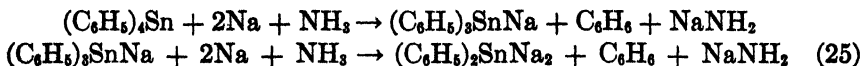
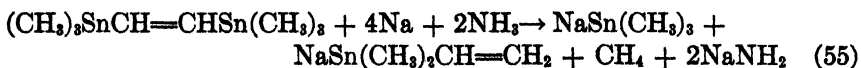
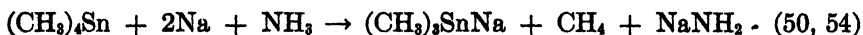
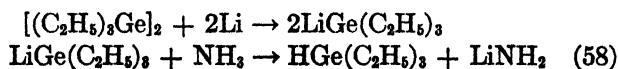
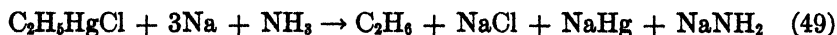
*Nitrogen compounds*



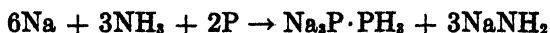
*Sulfides*



*Metallo-organic compounds*



A similar reaction in the inorganic field has also been reported (41):



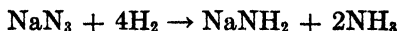
The alkali amides are also products of the ammonolysis of the monoxides,  $M_2O + NH_3 \rightarrow MNH_2 + MOH$  (75):  $NaNH_2$  (45, 52),  $KNH_2$  (52, cf. 60),  $CsNH_2$  (73, 74). This reaction is the initial one in the slow oxidation of the alkali metals in liquid ammonia. A closely related reaction is that of nitrous oxide upon solutions of sodium and potassium:



Finally, sodium nitride is ammonolyzed to the amide by gaseous or liquid ammonia (84):



Sodium amide has been reported as a reduction product of sodium azide (39, 88):



Patents dealing with the manufacture of the alkali amides include those covering the use of the catalysts previously mentioned, the preparation of a solution of sodium amide in sodium hydroxide (102), and the preparation of finely divided, reactive sodium amide (110) by stirring the amide in the presence of a diluent before it congeals.

#### V. PROPERTIES OF THE ALKALI AMIDES

Mentrel (66) has given the following observations on the behavior of the alkali amides: Molten sodium amide in contact with gaseous ammonia is a bright green liquid. At 500°C. it darkens and vigorously evolves nitrogen and hydrogen; the amide is regenerated upon cooling in an ammonia atmosphere. In a vacuum decomposition begins at 330°C. and is complete at 440°C., sodium metal remaining. At 390°C. gas evolution is slow and a mixture of sodium nitride (?), sodium, and sodium amide is left. Below 400°C. lithium amide is a bright green liquid, becoming reddish at 430°C. and evolving nitrogen and hydrogen. In a vacuum gassing begins at 370°C.; at 450°C. lithium imide, or a mixture of the nitride and amide, is left. Between 750° and 800°C. decomposition into lithium and ammonia is complete. Lithium and lithium amide in a vacuum at 460°C. do not give the imide.

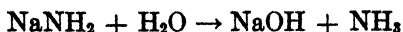
Patents have been issued for the preparation of water-free caustic alkalis by the action of water on the alkali metal amides (100). In the preparation of metallic sodium by the electrolysis of fused sodium hydroxide, Moltkehanen (109) claims that the addition of sodium amide has a desirable effect. The presence of sodium amide not only lowers the melting point of the electrolyte bath very much, but also suppresses the



secondary reaction between sodium and water at the cathode with formation of hydrogen. Instead of diffusing through the electrolyte, the water arising from the discharge of the hydroxyl ion,



is fixed with the liberation of ammonia,



As a result of greatly improved methods, older values for the conductances of the amides of sodium and potassium in liquid ammonia have been corrected by the work of Hawes (38; cf. 57) and the concentration range has been extended. The data obtained for sodium amide do not agree with the simple mass action or more refined theories, possibly because of the small size of the amide ion. Somewhat better agreement was found in the case of potassium amide.

Whereas Franklin (33) has given the solubility of sodium amide as 1 g. per liter (14, p. 60), Hunt and Boncyk (42) report the value of 0.004 g. per 100 g. of ammonia. Since the latter determination was made on a commercial sample (usually very impure) of the amide (43), the result may well be questioned. The validity of Franklin's value is substantiated by the conductance work of Hawes (38), who found that at  $-33^\circ\text{C}$ . saturation is attained at approximately 50 liters (0.8 g. of sodium amide per 1000 cc. of ammonia). A variety of sodium amide has been reported which is soluble to the extent of approximately 1 mole per liter at  $-33^\circ\text{C}$ . (82). The solubility of potassium amide at  $25^\circ\text{C}$ . is given as 3.6 g. per 100 g. of ammonia (42).

#### VI. DETERIORATION OF THE AMIDES DURING STORAGE

Bouveault and Levallois (17) state: "It is highly desirable to powder sodium amide under dry ether or benzene. For lack of this precaution we had a rather curious accident. When the amide contains some sodium nitrite (which is not rare) and accidentally a bit of sodium, the rise in temperature produced by grinding in the presence of air produces a violent combustion." Other investigators (40) report that sodium amide kept poorly sealed explodes when fused with organic substances. These observations support the recommendations previously made (14, pp. 64-5) for storing the amides. A patent (112) has been granted for the preparation of mixtures which can be safely handled and transported by grinding an alkali amide with two to six times its weight of an inert organic liquid, e.g., benzene, until a homogeneous paste is obtained.

## VIII. THE NATURE OF THE FUSED AMIDES

A patent has been granted for the preparation of the alkali metals by the electrolysis of their molten amides (101).

## IX. REACTIONS OF THE ELEMENTS WITH THE ALKALI AMIDES

*Group I, Subgroup B*

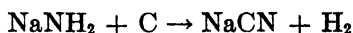
*Copper.* Vessels of copper are not attacked by fused sodium amide (78).

*Group II, Subgroup B*

*Indium.* Indium is not attacked by a solution of potassium amide in liquid ammonia (29).

*Group IV, Subgroup B*

*Carbon.* Perhaps the earliest reference to the formation of cyanides by the action of carbon upon sodium amide is that of Drechsel (28), who gives the equation



He also states that potassium cyanamide is reduced to the cyanide by carbon.

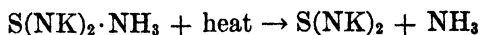
*Germanium.* Germanium is not attacked by a liquid ammonia solution of potassium amide (97).

*Tin; lead.* Bergstrom's work on the action of liquid ammonia solutions of potassium amide upon tin and lead has recently been confirmed (97).

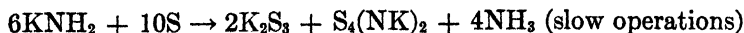
*Group VI, Subgroup B*

*Sulfur.* The following reactions have been found to occur at  $-33^\circ\text{C}$ . between potassium amide and sulfur in liquid ammonia solution (15):

Potassium amide in excess:



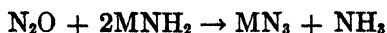
Sulfur in excess:

*Group VII, Subgroup B*

*Iodine.* Ruff (76) reports the formation of a salt,  $\text{Na}_2\text{NI}_3$ , when sodium amide and iodine react in liquid ammonia.

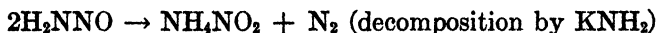
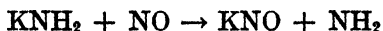
## X. REACTIONS OF THE ALKALI AMIDES WITH COMPOUNDS

The reaction,

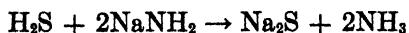
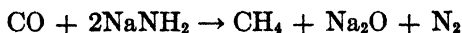


takes place in liquid ammonia with both sodium and potassium amides (46, 48; cf. 5). The reaction between finely divided sodium amide and nitrous oxide is used for the commercial preparation of azides (104, 108, 111).

Nitric oxide, under pressure, reacts with potassium amide in solid ammonia to give a series of products which may be regarded as arising through the following reactions (79):



Sodium amide has been used to free a mixture of gaseous hydrogen and nitrogen from traces of moisture, carbon monoxide, and hydrogen sulfide (26). The following reactions are said to take place at 100°C.:



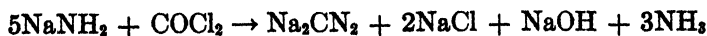
Liquid ammonia, sodium amide, and compressed carbon monoxide are reported to give the sodium salts of hydrocyanic, carbonic, and formic acids (80). On mild heating sodium amide converts potassium cyanate into a salt of cyanamide (28),



At ordinary temperature, sodium amide reacts slowly with carbonyl chloride (in toluene solution) according to the equation,

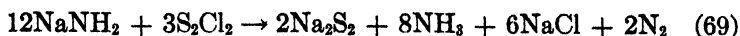


(see p. 431). At 250°C. the reaction is the following,

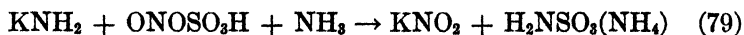


although the product contains 13 to 14 per cent of  $\text{NH}_4\text{CN}$ . At 500°C. inflammation occurs with formation of melanurates and their chloro

derivatives (69, 70). With sulfuryl chloride,  $\text{SO}_2\text{Cl}_2$ , in toluene solution a 20 per cent yield of trisulfimide results, but no sulfamide. Similarly, with sulfur monochloride in xylene at ordinary temperature, sulfur and sulfur nitride are formed, but at  $120^\circ\text{C}$ ., in the absence of air, the reaction is represented by



The compound  $\text{N}:\text{SH}\cdot\text{N}:\text{SH}\cdot\text{N}:\text{SH}\cdot\text{N}:\text{SH}$  (tetrathiolotetrazole) forms with potassium amide in liquid ammonia a compound,  $\text{KSN}\cdot\text{KNH}_2$ , which is freely soluble in the ammonia if an excess of  $(\text{HSN})_4$  is present. So much potassium amide is invariably present in equilibrium that addition of lead iodide precipitates a mixture of  $\text{Pb}(\text{SN})_2\cdot\text{NH}_3$  with  $\text{PbNH}$  and  $\text{PbN}\cdot\text{PbI}\cdot\text{NH}_3$  (67). The following reactions also have been shown to occur:



Franklin (32; cf. 5) has demonstrated that azides may be obtained by heating liquid ammonia solutions of nitrates with the alkali amides. At  $80$ – $90^\circ\text{C}$ . potassium nitrate and potassium amide react thus:



Better yields (up to 75 per cent), in a shorter time, result from operating at a higher temperature ( $130$ – $140^\circ\text{C}$ ). At  $200^\circ\text{C}$ . or higher, liberal quantities of nitrogen are set free and the yield of potassium azide is lower. By using sodium nitrate and sodium amide, yields of sodium azide up to 16 per cent may be obtained. An 80 per cent yield of lead azide is achieved by heating lead nitrate with an excess of potassium amide in liquid ammonia solution. Stannous chloride forms sodium stannite in molten sodium amide,



Sodium amide reacts with anhydrous hydrazine to give a very unstable salt,  $\text{NaNH}\cdot\text{NH}_2$  (81, 85). Sodium amide (not in excess) liberates only trivial amounts of hydrazine from hydrazinium salts (44) in hydrocarbon media.

If silicates, glasses, and certain refractories are ground to pass through a 200-mesh sieve, they can be decomposed by fusion with sodium amide at

300–337°C. A 100-cc. nickel crucible is recommended and an electric muffle through which ammonia gas is passed. After fusing, a complete analysis may be made in the usual way (71).

Lock (65) found that a considerable quantity of gas was evolved when sodium amide was heated to 150°C. in glass vessels.

The reaction of sodium amide with cyanogen is discussed in part II, section XII F (see p. 458).

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- (99) ASAKI GARASU, K. K.: French patent 793,150; Chem. Abstracts **30**, 4102 (1936).
- (100) ASHCROFT, E. A.: British patent 1,004; Chem. Abstracts **7**, 2288 (1913). German patent 268,826; Chem. Zentr. **1914**, I, 505.
- (101) ASHCROFT, E. A.: German patent 323,004; Chem. Zentr. **1920**, IV, 525.
- (102) Badische Anilin und Soda-Fabrik: German patent 323,656; Chem. Zentr. **1920**, IV, 431.
- (103) Deutsche Gold-und-Silber-Scheide-Anstalt vorm. Roessler: British patent 1,613; Chem. Abstracts **10**, 1917 (1916). Swiss patent 74,226; Chem. Abstracts **11**, 1890 (1917). Swiss patents 76,038-40; Chem. Abstracts **12**, 1111 (1918).
- (104) Dynamit-A.-G. vorm A. Nobel and Co.: German patent 619,753; Chem. Abstracts **30**, 1527 (1936).
- (105) EWAN, T.: U. S. patent 1,570,467; Chem. Abstracts **20**, 714 (1926).
- (106) HARA, R., AND ABE, S.: British patent 441,753; Chem. Abstracts **30**, 4102 (1936).
- (107) LIEBKNECHT, O.: U. S. patent 1,359,080; Chem. Abstracts **15**, 415 (1921).
- (108) MEISSNER, J.: French patent 723,416; Chem. Abstracts **26**, 4138 (1932).  
British patent 369,529; Chem. Abstracts **27**, 2255 (1933).
- (109) MOLTKEHANSEN, I. J.: French patent 777,001; Chem. Abstracts **29**, 3611 (1935).  
British patent 440,139; Chem. Abstracts **30**, 3951 (1936). Cf. Chem. Industries **39**, 269-71 (1936); J. Chem. Education **13**, 596 (1936).
- (110) The Pyridium Corp.: German patent 561,814; Chem. Abstracts **27**, 1108 (1933).  
VASIL'EV, B. B.: See Akhumov, E. I.  
VOÏNILOVICH, G. I.: See Akhumov, E. I.



- (111) Westfälisch-Anhaltische Sprengstoff-A.-G. chem. Fab.: German patent 619,017; Chem. Abstracts **30**, 582 (1936).  
 (112) ZIEGLER, K.: German patent 601,047; Chem. Abstracts **28**, 7439 (1934).

Important articles appearing too late for inclusion in this review are:

- JUZA, R.: Z. anorg. allgem. Chem. **231**, 121-35 (1937). Amides of the first and second groups of the periodic system.  
 SAKURAZAWA, K., AND HARA, R.: J. Soc. Chem. Ind., Japan **39**, Suppl. binding 491 (1936); **40**, Suppl. binding 10 (1937); Chem. Abstracts **31**, 5113<sup>a</sup> (1937). The synthesis of sodium amide from its elements and its thermal decomposition.

Certain additions and corrections should be made in connection with the references given in the earlier paper (14, pp. 80-2):

- Ref. 2. Add: BEILSTEIN, F., AND GEUTHER, A.: Jahresber. **1858**, 118-21.  
 Ref. 4. Add: BERGSTROM, F. W.: Science **53**, 578 (1922).  
 Ref. 12. Add: cf. KRAUS, C. A.: Trans. Am. Electrochem. Soc. **45**, 184-6 (1924).  
 Ref. 26. Add: DENNIS, L. M., AND BROWNE, A. W.: Z. anorg. Chem. **40**, 82-94 (1904).  
 Ref. 64. Add: JOANNIS, A.: Compt. rend. **112**, 392 (1881).  
 Ref. 74. Change to: OGG, R. A., JR., LEIGHTON, P. A., AND BERGSTROM, F. W.: J. Am. Chem. Soc. **55**, 1754-66 (1933).  
 Ref. 106. Add: ACKER, C. E.: U. S. patent 914,100; Chem. Abstracts **3**, 1369 (1909).  
 Ref. 107. Add: ASHCROFT, E. A.: British patents 1,001-3, 1,005; Chem. Abstracts **7**, 2163, 2288 (1913). U. S. patent 1,163,498; Chem. Abstracts **10**, 315 (1916).  
 Ref. 109. Change Chem. Abstracts **10**, 2967 (1916) to Chem. Abstracts **10**, 1917 (1916).  
 Add: Austrian patent 87,461; Chem. Zentr. **1922**, IV, 541. German patent 316,137; Chem. Zentr. **1920**, II, 173.  
 Ref. 110. Add: EWAN, T.: German patent 411,732; Chem. Zentr. **1925**, I, 2648.

## PART II. ORGANIC REACTIONS

### I. INTRODUCTION. PREPARATION

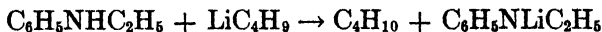
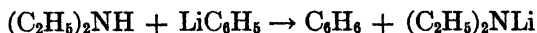
In bringing the review of the chemistry of the alkali amides (6) up to date, it has become apparent that it will be impossible to include all significant references to the literature, because of the difficulty of finding many of the articles which deal only incidentally with this subject. This is particularly true of the organic section. The authors sincerely hope that omissions will be brought to their attention.

Methods of preparing sodium amide have been discussed in the inorganic section of this review (part I), but the following appear to be of interest particularly to organic chemists. Ziegler (165) ground sodium amide with benzene or a similar inert hydrocarbon in a ball mill, obtaining a pasty mass which was very reactive and could be safely transported (cf. 6, p. 137). Shreve (136) has used a steel ball mill for making sodium amide and for the preparation from it of mono- and di-aminopyridines.

Vaughn, Vogt, and Nieuwland (149) have prepared a very reactive sodium amide by adding sodium to a solution of a small quantity of hydrated ferric nitrate in liquid ammonia (see also 126).

Organic substitution products of the alkali metal amides, of the type of lithium diethylamide  $(C_2H_5)_2NLi$ , have proven to be of considerable value in the preparation of branched-chain aliphatic nitriles, and in the synthesis of large ring systems, such as cyclopentadecanone (see section XII F).

Lithium salts of the primary and secondary aliphatic and secondary aliphatic-aromatic amines are most easily prepared on a laboratory scale by treating the amine with a solution of lithium phenyl or lithium *n*-butyl in absolute ether (166; cf. 6, p. 137). Thus,



Large scale manufacture, however, demands a cheaper method of preparation, and consequently we find several patents in this field during the past few years.

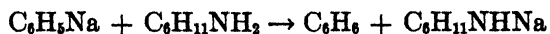
According to Ziegler (161), compounds of the formula  $MNRR'$  ( $M$  is an alkali metal,  $R$  is an aliphatic or aromatic radical, and  $R'$  is hydrogen or an aliphatic or aromatic radical) are prepared by treating an alkali metal with a primary or secondary aliphatic or secondary aliphatic-aromatic amine in the presence of (a) an alkyl or aryl halide, (b) an unsaturated hydrocarbon having at least two conjugated double bonds, (c) an unsaturated hydrocarbon having an aryl residuc linked to an unsaturated carbon atom, or (d) an aromatic hydrocarbon capable of forming addition products with the alkali metals.

Thus lithium, diethylamine, and naphthalene react in ether (atmosphere of nitrogen) to give lithium diethylamide,  $(C_2H_5)_2NLi$ . Lithium, monoethylaniline, and styrene or butadiene give lithium ethylphenylamide,  $C_6H_5N(Li)C_2H_5$ . Sodium cyclohexylamide,  $C_6H_{11}NHNa$ , may be made from sodium, cyclohexylamine, and phenyl chloride.

Lithium and naphthalene react to form an addition compound, which is "aminolyzed" by diethylamine to lithium diethylamide, in the same way that the substance formed by treating naphthalene with sodium in liquid ammonia is ammonolyzed to tetrahydronaphthalene and sodium amide (159, 97a).

The alkali metals add to many double bonds, and particularly to those activated by aryl groups. These addition compounds are "aminolyzed" to metallic derivatives of the amine and the reduced hydrocarbon. Phenyl chloride and sodium in ether are known to give the highly reactive sodium

phenyl (110a), and this is doubtless the immediate precursor of sodium cyclohexylamide.



## II. THE OXIDES OF CARBON AND CARBON DISULFIDE

Carbon monoxide is treated in part I, section X. Carbon disulfide is mentioned in part II, section VIII B.

## III. AMMONOCARBONIC ACIDS

The dialkyl cyanamides,  $\text{R}_2\text{NCN}$ , are esters of cyanamide,  $\text{NH}_2\text{CN}$ , an ammonocarbonic acid, and will be considered under section XIII A.

Niemann (as reported by Franklin (47)) found that *N*, *N'*, *N''*-triphenylguanidine (a triphenyl ester of an ammonocarbonic acid, guanidine) forms a dipotassium salt with potassium amide in liquid ammonia at room temperatures, but no further reaction occurs on heating, although one should anticipate ammonolysis to guanidine and aniline. This may, however, be brought about by ammonium chloride in liquid ammonia at 200°C.

Biechler (9) has studied the reactions,



and



The first reaction is to be interpreted as the action of a base, sodium amide, on an acid bromide of an ammonocarbonic acid, cyanogen bromide, to give the salt of an ammonocarbonic acid, sodium dicyanimide. Apparently, under the conditions of Biechler's work, the latter is not changed to disodium cyanamide,  $\text{Na}_2\text{CN}_2$ , as in the work of Perret and Perrot (118). Phenyldicyanoimide, *o*-methoxyphenyldicyanoimide, and *p*-tolylidicyanoimide were prepared in accordance with the second equation, but attempts to make the corresponding *o*-tolyl, chlorophenyl, and  $\alpha$ -naphthyl derivatives failed. (A mixture of polymers was obtained.)

## IV. MIXED AQUOAMMONOCARBONIC ACIDS

Potassium cyanate is treated in part I, section X. Blair and Smith (105), in accumulating evidence for the tautomerism of cyanourea,  $\text{NH}_2\text{CONHCN}$ , have prepared an ammonia-soluble monopotassium salt and ammonia-insoluble di- and tri-potassium salts by the action of potassium amide in proper proportion on this aquoammonocarbonic acid in liquid ammonia. The work of Miss Fulton, concerning the formation of

monopotassium and monosodium salts of the acid amides in liquid ammonia, and their decomposition into hydrocarbons at elevated temperatures when heated with an excess of alkali amide, has now been published (47a).

Perret and Perrot (118, 119) give the following equations for the reaction between phosgene and sodium amide (see p. 422). In toluene, at ordinary temperatures,



At 250°C., the chief reaction is



but the product contains 13 to 14 per cent of  $\text{NH}_4\text{CN}$ .

#### V. HYDROCARBONS (ALL CLASSES)

Cook and Hewett (28a) find that 2,3-benzo-1,3,3-bicyclo- $\Delta^2$ -nonene does not react with methyl iodide and sodium amide.

Carothers and Jacobson (15, 80) have prepared the sodium salt of vinylacetylene,  $\text{CH}_2=\text{CHC}\equiv\text{CNa}$ , with the use of sodium amide, and from it have made 1-(methyl, ethyl, butyl, or heptyl)-2-vinylacetylene.

Lai (96) prepared the sodium salt of *n*-heptyne,  $\text{CH}_3(\text{CH}_2)_4\text{C}\equiv\text{CNa}$ , by the action of sodium amide on *n*-heptyne in xylene at 60°C. From this, and from the sodium salts of *n*-octyne and *n*-undecyne, a number of diacetylenes were made by the reaction represented below.



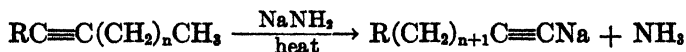
Among other compounds, the following were made: heptadecadiyne-7,10; hexadecadiyne-6,9; pentadecadiyne-6,9; and tricosadiyne-6,9. The poor yields (about 20 per cent) were due not only to resinification, but also to the formation of tri- or tetra-acetylenic hydrocarbons.

Mlle. Grédy (56), in connection with her work on Raman spectra, has alkylated the sodium salts of a number of acetylenic hydrocarbons with dimethyl sulfate. A few of the compounds prepared in this manner are 1-cyclopentyl-1-propyne, 1-cyclohexyl-1-propyne, pentyne-2, hexyne-2, heptyne-2, octyne-2, nonyne-2, and 3-phenylpropyne-2.

Bried and Hennion (12b) have prepared diethyl-, dipropyl-, dibutyl-, and diamyl-acetylenes by the action of the corresponding alkyl halide on sodium acetylide and sodium amide in liquid ammonia, without the isolation of the intermediate monoalkylacetylenes.

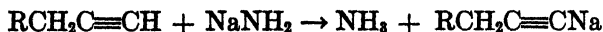
Vaughn (148a) has prepared propyl-, butyl-, heptyl-, and nonyl-acetylenes from the corresponding alkyl halide and the sodium salt of acetylene in liquid ammonia.

There are recorded a few new illustrations of the Favorsky rearrangement,



in which a disubstituted acetylene is converted by the action of sodium amide at elevated temperatures in an inert medium (mineral oil, etc.) into the sodium salt of a "true" acetylene.

According to Lai (97), the action of sodium amide on tetracos-10,14-diyne at 160–170°C. liberated ammonia corresponding to a 60 per cent transformation of the diacetylene into an isomeric "true" acetylene. The extreme instability of the latter and consequent resinification prevented its isolation. The isomerization by sodium amide is due to its tendency to form an insoluble salt with the "true" acetylene, and thus the equilibrium mixture of  $\text{RC}\equiv\text{CCH}_3$  and  $\text{RCH}_2\text{C}\equiv\text{CH}$ , for example, passes into an irreversible system,



Since Vaughn, Vogt, and Nieuwland (149) were unable to rearrange ethylamylacetylene with sodium amide in liquid ammonia at  $-33^\circ\text{C}$ . in sixteen hours, a high temperature is apparently necessary. Decylacetylene was prepared in 34 per cent yield by heating diamylacetylene with sodium amide in mineral oil at  $210^\circ\text{C}$ ., while octylacetylene was similarly prepared from dibutylacetylene (148a).

Guest (58, 59) states that both true acetylenes (i.e., those which contain a  $\equiv\text{CH}$  group) and isoacetylenes (of the type  $\text{RC}\equiv\text{CR}'$ ) are formed by heating paraffin dihalides with sodium amide; this statement is in disagreement with the views of Bourguet (11), who claims that only true acetylenes are formed. *n*-Heptyne,  $\text{CH}_3(\text{CH}_2)_4\text{C}\equiv\text{CH}$ , was rearranged by passing over heated soda lime to a mixture containing a large proportion of isoheptynes. Heated sodium amide, under mineral oil, altered the composition of this mixture to about 65 per cent of the true heptyne.

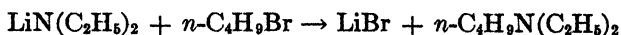
Kraus and Kahler (93) have made sodium triphenylmethyl,  $(\text{C}_6\text{H}_5)_3\text{CNa}$ , for conductivity work by the action of sodium amide on triphenylmethane in liquid ammonia.

The action of sodium amide on fluorene (at  $150^\circ\text{C}$ .) and indene (at  $110$ – $115^\circ\text{C}$ .) gives the corresponding sodium salts (151, 152). Advantage has been taken of this in the separation of fluorene from the coal tar fraction in which it is contained, and in its purification (51). A process has been patented for the preparation of sodium indene with the use of sodium amide or sodium metal and dry ammonia (52).

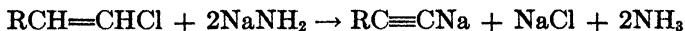
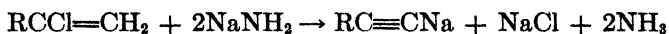
## VI. HALOGEN COMPOUNDS

A. *Paraffin monohalides*

Horning (74) obtained cyclohexene in 65 per cent yield by treating cyclohexyl chloride with potassium amide in liquid ammonia. He also prepared diethyl-*n*-butylamine in absolute ether in accordance with the equation,

B. *Unsaturated monohalides*

A very convenient method for preparing acetylenic hydrocarbons has been discussed in the previous review (6, pp. 92-8), and is expressed by the equations,



If the reaction yields a disubstituted acetylene, with at least one of the substituents an alkyl group, the Favorsky rearrangement may occur, yielding a true acetylene (see section V).

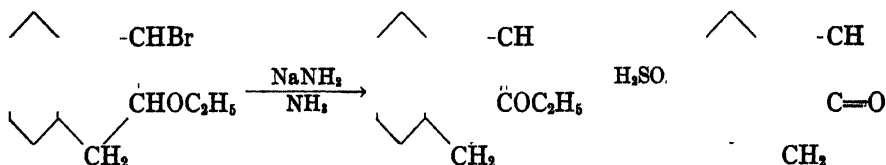
Thus, Davis and Marvel (34) prepared 3-ethyl-3-methylpentyne-1 in 75 per cent yield by heating sodium amide with 3-ethyl-3-methyl-2-chloropentene-1 in mineral oil at 160-175°C. Ozanne and Marvel (117) have used the method of Lespieau and Bourguel (98) to prepare  $(\text{CH}_3)_3\text{CCH}_2\text{C}\equiv\text{CH}$  from  $(\text{CH}_3)_3\text{CCH}_2\text{CBr}=\text{CH}_2$  and sodium amide. Mlle. Grédy (56, 57) treated the mixture of halides resulting from the action of phosphorus pentachloride on methyl isopropyl ketone with sodium amide at 150°C., obtaining isopropylacetylene in poor yield. Guest (58, 59) has made use of this method in the synthesis of some acetylenes, as has previously been described in section V. Lewinsohn (99) similarly prepared *n*-heptyne.

According to Vaughn, Vogt, and Nieuwland (149), sodium amide, prepared in liquid ammonia at -33°C. by the action of ammonia on sodium in the presence of hydrated ferric nitrate as a catalyst, readily removes hydrogen halide from suitably constituted compounds to give acetylenes. Thus, 2-bromoöctene-1 is converted in 73 per cent yield to hexylacetylene,  $\beta$ -bromostyrene in 75 per cent yield to phenylacetylene, and 2-iodohexene-1 in 31 per cent yield to *n*-butylacetylene.

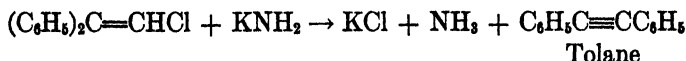
Mlle. Grédy (57) has used the sodium amide method for the preparation of a number of acetylenic hydrocarbons from unsaturated halides, having synthesized, among other compounds, the following: isopropylacetylene

from  $(\text{CH}_3)_2\text{CHCBr}=\text{CH}_2$ , 3-cyclopentyl-1-propyne from 3-cyclopentyl-2-bromo- $\Delta^1$ -propene (in decalin), and cyclohexylacetylene.

Porter and Suter (122) removed the elements of hydrobromic acid from 1-ethoxy-2-bromoindane with sodium amide in liquid ammonia at  $-33^\circ\text{C}$ ., forming an enol ether, which gave 1-indanone after hydrolysis.



Coleman, with Maxwell and Holst, has examined the reaction of potassium amide, dissolved in liquid ammonia, with a number of chloroethenes and bromoethenes. In all cases hydrogen halide is readily removed, but in so doing there is a rearrangement to give a substituted tolane, or di-phenylacetylene. Thus,



An *o*-, *m*-, or *p*-substituted phenyl in the chloro- or bromo-ethene appears in the same configuration in the product. As an illustration, 1,1-di-*o*-tolylbromoethene and potassium amide give di-*o*-tolylacetylene.

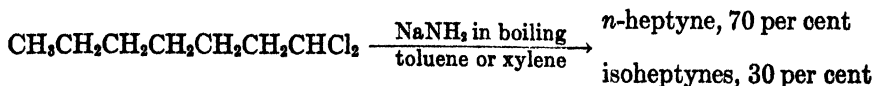
These reactions are interpreted as involving, first, the removal of halide ion from the diarylchloro- or bromo-ethene, leaving a carbon atom with a sextet of electrons. A pair of electrons is attracted from the neighboring carbon atom, the aryl group held by the shifting electrons moving with it. An electron pair then shifts to give a triple bond, liberating a proton and forming the tolane. The yields of crude tolanes exceeded 90 per cent of the theoretical, with the exception of those containing *p*-ethylphenyl, *p*-*n*-propylphenyl, and *p*-*n*-butylphenyl groups, where 60 per cent appeared to be the maximum yield (26, 27, 28).

### C. Paraffin polyhalides

Dihalides of the type of ethylene dibromide, with halogens on adjacent carbon atoms, in general react with the alkali amides to form acetylenes. Thus, Vaughn, Vogt, and Nieuwland (149) have made stilbene from stilbene dibromide and sodium amide in liquid ammonia in 86 per cent yield. *n*-Amylacetylene and *n*-octylacetylene are similarly formed in approximately 55 per cent yield from 1,2-dibromoheptane and 1,2-dibromodecane, respectively.

Guest (58), in disagreement with Bourguet (11), finds that sodium amide

reacts with dihalides to give isoacetylenes as well as "true" acetylenes, as in the reaction,



1,2-Dibromobutane reacts with sodium amide in kerosene at 145°C. to give the sodium salt of an acetylene, which, after carbonation, becomes ethylpropionic acid,  $\text{C}_2\text{H}_5\text{C}\equiv\text{CCOOH}$  (42) (2 to 3 per cent yield).

Titanium trichloride and *tert*-butylethinylcarbinol react to form a dihalide,  $\text{C}_{38}\text{H}_{54}\text{Cl}_2$ , which, with sodium amide in xylene, gives a hydrocarbon,  $\text{C}_{38}\text{H}_{54}$ , of unknown constitution (144).

Propylidene dichloride and sodium amide in paraffin oil give methylacetylene in poor yield (75).

Divinyl ether is formed only to the extent of 3 per cent by the action of sodium amide on  $\beta,\beta'$ -dichloro(or diiodo)ethyl ether in xylene at its boiling point (125). Hexafluoroethane reacts violently with sodium amide at 250°C., but no products have been isolated (143).

#### D. Aromatic halides

Phenylacetylene is formed in yields of 75 per cent and 57 per cent, respectively, by treating  $\beta$ -bromostyrene and  $\alpha$ -chlorostyrene with sodium amide in liquid ammonia (149).

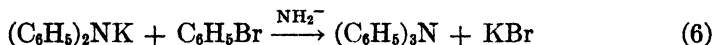
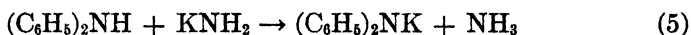
According to a German patent (105), chlorobenzene reacts with sodium amide at 110–120°C., in the presence of copper gauze or copper powder, to give triphenylamine, while under similar conditions tribenzylamine is obtained from benzyl chloride and triisamylamine from isoamyl chloride. Mixtures of chlorine compounds and a primary amine may be heated with sodium amide, when, if the amine contains a different radical, a mixed tertiary amine results. Thus, benzyl chloride and *p*-toluidine give dibenzyl-*p*-toluidine, while aniline and benzyl chloride give dibenzylaniline. On the other hand, a solution of potassium amide in liquid ammonia converts benzyl chloride either to stilbene,  $\text{C}_6\text{H}_5\text{CH}=\text{CHC}_6\text{H}_5$ , or to a compound of the composition  $(\text{C}_7\text{H}_8)_4$  and m.p. 144°C., depending upon the conditions. Other substances are formed in this reaction, whose mechanism is at present imperfectly understood (124, 148).

Chloro-, bromo-, and iodo-benzenes (fluorobenzene is inert) react very rapidly with a liquid ammonia solution of potassium amide at -33°C. to give aniline and diphenylamine, with smaller quantities of triphenylamine and *p*-aminobiphenyl, in proportions which depend upon the experimental conditions (7). In boiling ether or benzene the above reactions either do not occur, or else are very slow.



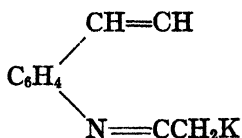
The formation of potassium anilide, or potassium diphenylamide, in accordance with equations 1 and 5 below is very rapid in comparison with the primary replacement of halogen (equation 1). Consequently, when potassium amide is added to an excess of a phenyl halide, halide ion is formed only to the extent of 50 to 60 per cent of the theoretical, calculated on the basis of the potassium. Competition reactions indicate the following order of ease of replacement of halogen in the unsubstituted phenyl halides:  $\text{Br} > \text{I} > \text{Cl} > > > \text{F}$ . The same order is found for replacements involving the phenyl dihalides of the type  $p\text{-C}_6\text{H}_4\text{XY}$ .

The reactions, insofar as is known at the present time, are expressed by the following equations (160),



It is interesting to observe that reactions 3, 4, and 6 are rapid only in the presence of an excess of amide ions, that is to say, of an excess of potassium amide. This peculiar form of catalysis has yet to receive a satisfactory explanation.

Potassium triphenylmethyl,  $(\text{C}_6\text{H}_5)_3\text{CK}$ , reacts more rapidly with chlorobenzene in the presence of potassium amide than in its absence, tetraphenylmethane,  $(\text{C}_6\text{H}_5)_4\text{C}$ , being formed. Addition of potassium amide to a solution of chlorobenzene and potassium quinaldyl,



in liquid ammonia gives 2-benzylquinoline, 2-benzohydrylquinoline, and 2-triphenylmethylquinoline, all three hydrogen atoms of the methyl group of quinaldine having been replaced by phenyl. The structure of the last two has not yet been proven by independent synthesis.

Only the strongest bases in the Brønsted sense (i.e., the strongest anions),  $\text{NH}_2^-$ ,  $(\text{C}_6\text{H}_5)_2\text{CH}^-$ , and  $(\text{C}_6\text{H}_5)_3\text{C}^-$ , react with the phenyl halides in

liquid ammonia at  $-33^{\circ}\text{C}.$ , and the last two only react slowly. The strongest base of those examined,  $\text{NH}_2^-$ , alone catalyzes reactions of the type discussed, although it will probably be found that  $(\text{C}_6\text{H}_5)_2\text{CH}^-$  also does so.

Horning (74), in extending these investigations, finds that *p*-phenetidine may be prepared in 31 per cent yield by treating *p*-chlorophenetole with potassium amide in liquid ammonia. Many other aryl halides (such as *p*-chloroanisole, 2-bromopyridine, 2-chloroquinoline, and *p*-chlorophenol at  $-33^{\circ}\text{C}.$ ) are converted largely to tar under the same conditions. Some halides, possibly because of unfavorable solubility relationships, react only to a slight extent or not at all with potassium amide at  $-33^{\circ}\text{C}.$  Among these are *p*-bromobiphenyl, sodium *p*-bromobenzenesulfonate, and *p*-iodobiphenyl.

Somewhat better results were observed in the reaction between the lithium alcoholates of the ammonia system— $\text{LiN}(\text{C}_2\text{H}_5)_2$  and  $\text{LiN}(n\text{-C}_4\text{H}_9)_2$ —with aryl chlorides or bromides in ethereal solution. From lithium diethylamide were prepared diethylaniline (60 to 92 per cent), *m*-methyldiethylaminobenzene (23 per cent), and *p*-methyldiethylaminobenzene (35 per cent). From lithium di-*n*-butylamide, di-*n*-butylaniline was made in 36 per cent yield, and from *N*-lithium piperidine, *N*-phenyl piperidine in 47 per cent yield.

#### VII. ALCOHOLS, PHENOLS, AND ETHERS

Phenols in a mixture have been determined by determining the ammonia evolved when they react with sodium amide (134). Benzohydrol, even with an excess of sodium amide in liquid ammonia, yields only the monosodium salt,  $(\text{C}_6\text{H}_5)_2\text{CHONa}$  (90), although Wooster (159a, first reference) states that a dipotassium benzohydrol,  $(\text{C}_6\text{H}_5)_2\text{CK}(\text{OK})$ , is formed by treating benzohydrol with potassium amide in the same solvent.

Renfrew and Cretcher (123) found that cinchonine and hydroquinine were oxidized to the corresponding ketones, cinchoninone and hydroquininone, by sodium amide in boiling xylene. In attempting to generalize this reaction, it was found that methylisobutylcarbinol was scarcely affected under the same conditions, nor was benzohydrol, except for the formation of an intense purple color (cf. 159a).

According to Mottier (111), sodium amide in tetralin at  $200\text{--}300^{\circ}\text{C}.$  splits the monomethyl ethers of pyrocatechol, resorcinol, and hydroquinone into the corresponding phenols in yields of 75 to 100 per cent, the best results being obtained at the higher temperature. The following were not split under the same conditions: the methyl ethers of phenol; the *o*-, *m*-, and *p*-cresols; the dimethyl ethers of pyrocatechol, resorcinol, and hydroquinone; and diphenyl oxide. Sartoretto and Sowa (128a) find

that the compound named last is not cleaved by sodium amide in liquid ammonia at  $-33^{\circ}\text{C}$ .

Helfer and Mottier (72a) state that in contact with sodium amide methylene pyrocatechol and some of its derivatives (e.g., safrole, dihydro-safrole) are colored blue. The color disappears on heating, and at a sufficiently high temperature a violent reaction occurs with evolution of gas. The corresponding diphenols can be isolated.

The sodium salts of the naphthols are best prepared in liquid ammonia by the action of sodium amide on the naphthol, since reduction products are formed when sodium is used (92).

Mlle. Grédy (57a) has used sodium amide in preparing the methyl ethers of a number of acetylenic alcohols. The following directions are typical: 40 g. of octyne-2-ol-1,  $\text{C}_8\text{H}_{11}\text{C}\equiv\text{CCH}_2\text{OH}$ , is converted by sodium amide in absolute ether to the sodium salt,  $\text{C}_8\text{H}_{11}\text{C}\equiv\text{CCH}_2\text{ONa}$ , in a rapid reaction. The ether is evaporated to remove ammonia formed in the reaction, and then a solution of 70 g. of dimethyl sulfate in ether is added, the mixture being gently heated for an hour. There is obtained in this manner an 80 per cent yield of the ether,  $\text{C}_8\text{H}_{11}\text{C}\equiv\text{CCH}_2\text{OCH}_3$ .

Sodium amide reacts with acetylenic alcohols of the type,

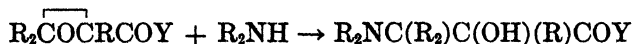


to form red sodium salts (57b). ( $\text{C}_6\text{H}_{11}$  is cyclohexyl.)

### VIII. AMINES

#### A. Aliphatic amines

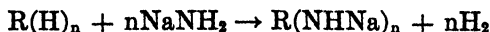
Glycidic acid, its esters, its amides, or their alkyl, aralkyl, or aryl substitution products are condensed with amines at elevated temperatures under substantially anhydrous conditions, in the manner of the following equation (sodium ethylate or sodium amide may be used as catalysts):



R is hydrogen, alkyl, aryl, or aralkyl. Y is OR or  $\text{NR}_2$ . With amines containing two reactive amino groups, such as  $\text{RNH}\cdot[\cdot]\cdot\text{NHR}$  (where  $[\cdot]$  is an

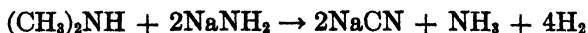
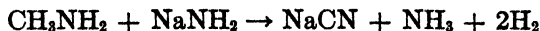
alkylene group or CO) products of the formula,  $\text{R}_2\text{CNR}\cdot[\cdot]\cdot\text{NRCOCR}(\text{OH})$  are obtained. Thus,  $\beta,\beta$ -dimethylglycidic acid, its amide or ethyl ester, with aniline or methylaniline and sodium amide give hydroxyanilino (or methylanilino) isovaleric acid, ester, or amide.  $\beta,\beta$ -Dimethylglycidic acid amide reacts with urea or phenylhydrazine in the presence of sodium amide to form 4,4-dimethyl-2,6-diketo-5-hydroxyhexahydropyrimidine or 1-phenyl-3,3-dimethyl-4-hydroxy-3,4-dihydro-5-pyrazolone, respectively (131).

Fry and Culp (49) have examined the action of fused sodium amide at 250°C. on mono-, di-, and tri-methylamines, and, as with reactions involving the fused alkali hydroxides, find that the following general equation is valid.

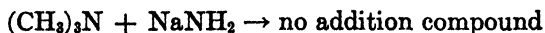
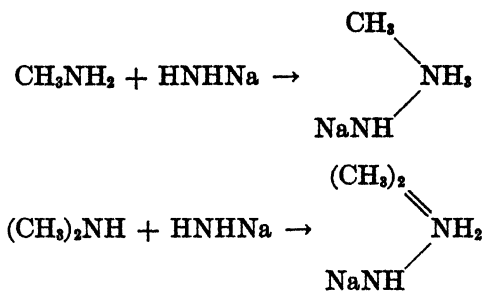


(Cf.  $R(H)_n + nNaOH \rightarrow R(ONa)_n + nH_2$ .)

Specifically,



The first two reactions, which take place to the extent of 95 per cent of the theory, are of the nitridation-reduction type, in which hydrogen gas appears in place of an organic reduction product. The methylamines have been nitridized to sodium cyanide. The following mechanism has been tentatively proposed.



The intermediate formation of an addition compound of the "ammonium" type is assumed to be necessary before further reaction can occur. Electronic formulas for the above cannot be constructed unless one nitrogen has a deficit of electrons.

It may be remarked that trimethylamine is an ether of the ammonia system and that its failure to react with sodium amide is analogous to the failure of aquo ethers to react with heated sodium hydroxide.

### B. Aromatic amines<sup>2</sup>

Wohl and Lange (155) used sodium amide to prepare a salt of aniline, which, without isolation, was used to make anilidoacetal,  $C_6H_5NHCH_2CH(OC_2H_5)_2$ .

<sup>2</sup> See also section I.

Kraus and Bien (90) state that it is impossible to prepare disodium phenylamide,  $C_6H_5NNa_2$ , by treating monosodium anilide with sodium amide in liquid ammonia. Monosodium anilide and monosodium diphenylamide have been made for conductance measurements in liquid ammonia by the action of sodium amide on aniline and diphenylamine, respectively.

Jones (80a) prepared a metallic derivative of a diarylamine, such as diphenylamine, in liquid ammonia, this solvent being replaced by toluene, and carbon disulfide introduced to give sodium diphenylthiocarbamate.

For the manufacture and use of compounds of the type of sodium diphenylamide, see section XII C (3a).

## IX. ALDEHYDES AND ALDEHYDE AMMONIAS

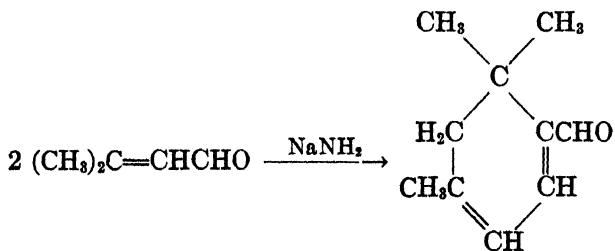
### A. Aliphatic aldehydes, hexamethylenetetramine

Sodium amide attacks the potassium salt of salicylaldehyde at 250–270°C., but the reaction was not of the Cannizzaro type, in that no salicylic acid was formed. A mixture of potassium hydroxide, sodium hydroxide, and a small amount of sodium amide, however, did react to give salicylic acid (101).

Kirssanov and Ivastchenko (88) suggest that the first step in the reaction between benzaldehyde and sodium amide (in which benzamide and benzyl alcohol are formed) is the addition of the sodium amide to the carbonyl group. Haller (62) has described a compound of the probable structure,  $(C_6H_5)_2C(ONa)NH_2$ , which was made from sodium amide and benzophenone.

Propionaldehyde, *n*-butyraldehyde, and *n*-heptaldehyde react with liquid ammonia to give viscous liquids, which do not seem to be affected by calcium amide (142).

Fischer and Löwenberg (46) have condensed 2-methylbutenal with a small amount of sodium amide in ether, and have obtained 1,1,5-trimethyl-2-formylcyclohexadiene-2,4 in 50 per cent yield.



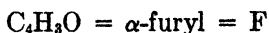
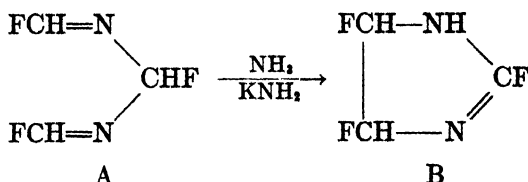
Apparently the presence of a branched-chain methyl in the  $\beta$ -position with respect to the  $-\text{CHO}$  group is necessary, since crotonaldehyde under similar conditions is converted only to resins. Citral, however, condenses readily in the manner of the above equation to yield a compound,  $\text{C}_{20}\text{H}_{30}\text{O}$ , which probably contains the same fundamental ring. 1,1,5-Trimethyl-2-formylcyclohexadiene and acetone react in the presence of sodium amide ( $3-25^\circ\text{C}.$ ) with loss of water. ( $-\text{CHO}$  in the above formula is replaced by  $-\text{CH}=\text{CHCOCH}_3$ .)

Hexamethylenetetramine,  $(\text{CH}_2)_6\text{N}_4$ , does not dissolve in liquid ammonia or in a heated solution of potassium amide in this solvent (142).

#### X. ALDIMINES, HYDRAMIDES, AND SCHIFF BASES

##### A. Hydramides

Strain (141) found that hydrofurfuramide (A) slowly dissolves in liquid ammonia to form furine (B), the reaction being greatly accelerated by adding very small quantities of potassium amide.



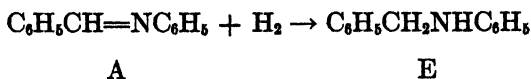
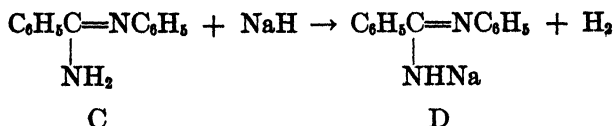
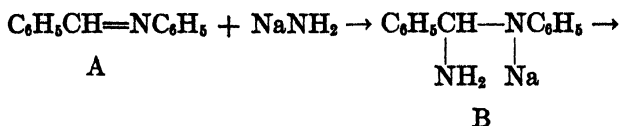
Hydrogen is liberated when furine (B) is treated with an excess of potassium amide in liquid ammonia, but the expected furyl compound corresponding to lophine was not isolated (cf. 6, p. 105).

##### B. Schiff bases

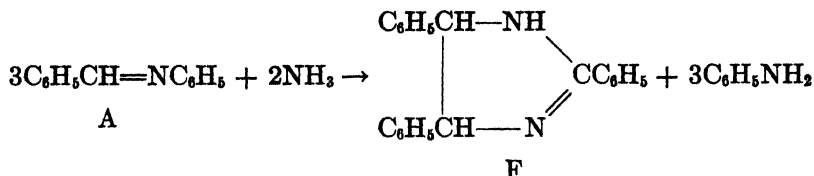
It has previously been found that an excess of potassium amide in liquid ammonia converts benzalaniline,  $\text{C}_6\text{H}_5\text{CH}=\text{NC}_6\text{H}_5$ , into benzylphenylbenzamidine,  $\text{C}_6\text{H}_5\text{C}(\text{NHC}_6\text{H}_5)=\text{NCH}_2\text{C}_6\text{H}_5$ , in a reaction of the Cannizzaro type (6, p. 105.) Apparently, polymeric Schiff bases result if the potassium amide is used in less than molar proportions.

Altering the experimental conditions, and avoiding the use of liquid ammonia, Kirssanov and Ivastchenko (87, 88) heated a number of Schiff bases with sodium amide under toluene, finding reactions of somewhat greater complexity than in liquid ammonia, as might be expected. Benzalaniline (A) is thus converted to aniline (12 per cent), phenylbenzamidine (C) (20 per cent), benzylaniline (E) (20 per cent), lophine (13 per cent),

and some colorless needles, melting at 207–8°C. The reaction is interpreted in the following manner.



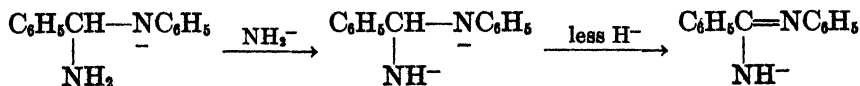
The lophine is probably obtained by the nitridation, or oxidation, of amarine (F), which is known to be formed by the action of alkali amides on hydrobenzamide (6, p. 105). The over-all reaction, expressing the formation of amarine, is the following,



The two hydrogens removed from amarine in forming lophine probably reduce benzalaniline (A  $\rightarrow$  E). No benzylphenylbenzamidine was isolated.

Benzal-*p*-toluidine and sodium amide under the same conditions give tolylbenzamidine (23 per cent), benzyltoluidine (21 per cent), lophine (13 per cent), and *p*-toluidine (13 per cent). Piperonylaniline is only partially attacked in the same length of time.

It will be seen that the interpretation of the reaction mechanism above is modelled after that of Ziegler and Zeiser (168), who have assumed the addition of sodium amide to the  $-\text{CH}=\text{N}-$  bond of pyridine and the loss of sodium hydride from the product to form 2-aminopyridine. The direct conversion of B to D could be brought about in the following manner (the reactions are written ionically):







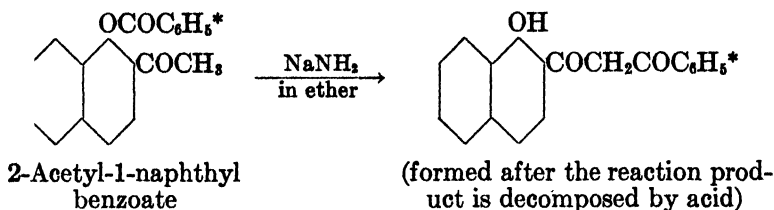
tion" of pinacolone, isobutyronone, and pentamethylacetone, with the result that the following compounds have been prepared: *n*-propylpinacolone, methyl-*n*-propylpinacolone, di-*n*-propylpinacolone, *n*-propylisobutyronone, pentamethyl-*n*-propylacetone, *s*-tetramethyl-di-*n*-propylacetone, *s*-dimethyldiethylacetone, 3,5-dimethyl-3-ethylheptanone-4, and a few others.

Propylation is definitely harder than methylation or ethylation and is best effected by the reaction between *n*-propyl iodide, sodium amide, and the ketone in boiling benzene.

### B. Mixed aliphatic-aromatic ketones

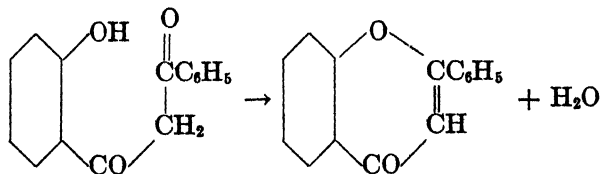
*s*-Dibenzylacetone, when treated with sodium amide and methyl iodide in ether (the process being repeated three times, benzene being used the last two times), gives tetramethyldibenzylacetone (60). Monobenzylacetone could not be successfully alkylated.

Mahal and Venkataraman (103) have discovered the rather peculiar reaction expressed by the equation,



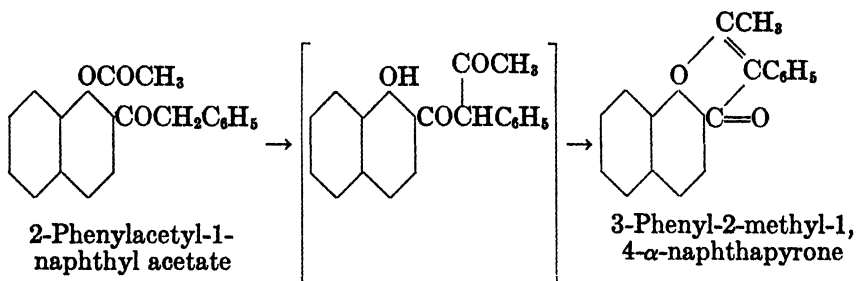
The phenyl group denoted by an asterisk may contain one, two, or three methoxyl groups.

In continuing this work, Bhalla, Mahal, and Venkataraman (8) treated *o*-benzoyloxyacetophenone, *o*-C<sub>6</sub>H<sub>5</sub>COOC<sub>6</sub>H<sub>4</sub>COCH<sub>3</sub>, with sodium amide in ether and obtained *o*-hydroxydibenzoylmethane, *o*-HOC<sub>6</sub>H<sub>4</sub>COCH<sub>2</sub>-COC<sub>6</sub>H<sub>5</sub>, as one of the reaction products. From this, by the action of sulfuric acid, a pyrone is formed, in accordance with the equation,



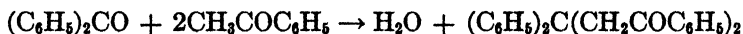
It is interesting that in many cases a pyrone is the product of the sodium amide reaction itself. Thus, 1-acetyl-2-naphthyl *o*-methoxybenzoate and 1-acetyl-2-naphthyl *p*-methoxycinnamate provide examples of the partial direct conversion into the pyrone. Substituents in the methyl group of

the ketone used in the reaction led chiefly to a pyrone, as in the following example:



Baker (2) has proposed a mechanism for rearrangements of this type.

de Carvalho (15a) has condensed acetophenone with benzophenone and with *p,p'*-dibromobenzophenone in the presence of sodium amide to diphenyldiphenacetylmethane, or its dibromo substitution product, in the manner of the equation,



3-Benzoyl-3-methylbutyric acid may be prepared in excellent yield by the reaction of ethyl iodoacetate with the sodium derivative of isopropyl phenyl ketone,  $\text{C}_6\text{H}_5\text{COCNa}(\text{CH}_3)_2$ , with saponification of the ester that is formed first. If ethyl chloroacetate is used instead of ethyl iodoacetate, a glycidic acid,  $(\text{CH}_3)_2\text{CHC}(\text{C}_6\text{H}_5)\text{OCHCOOH}$ , is formed (70; cf. 6, pp. 113-4).

Sodium amide converts 1,3-dibenzoylpropane in ether to a red disodium derivative, which may be alkylated with methyl iodide to 2,4-dibenzoylpentane. Alkylation of 1,3-dibenzoyl-2-phenylpropane does not give a stable product (3).

### C. Cyclic ketones

Sodium amide has been used in the alkylation of benzoylcyclopropane (69).

Dimethylindanone is formed by the action of methyl iodide on the reaction product of indanone and sodium amide (68).

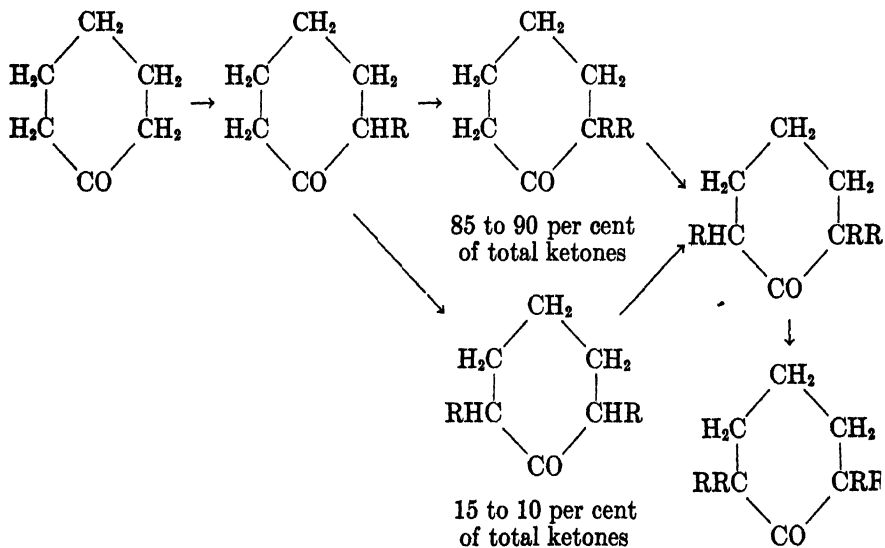
Rupe, Bürki, and Werdenberg (127) have used sodium amide in preparing sodium camphor, an intermediate in the synthesis of *d*-, *l*-, and racemic camphorcarboxylic acids. Thiocamphor is changed by sodium amide in ether at 0°C. to a sodium salt, and thence by reaction with amyl nitrite into isonitrosothiocamphor. The latter has been suggested as a reagent for the quantitative estimation of cobalt (135a). The sodium salt of camphor, prepared with the use of sodium amide, is converted to

oxymethylenecamphor by amyl formate (126). 4-Methylcamphor and sodium amide react in benzine (b. p. 100°C.) to give a sodium salt, which, with ethyl nitrite, gives methylisonitrosocamphor (113). Oddo (115) has used sodium amide in preparing sodium menthone, from which by carbonation he obtained menthonicarboxylic acid. He claims that the hydrolysis of the reaction product of sodium amide and camphor in toluene (temperature not stated) gives very little camphor, as would be anticipated if salt formation alone had occurred. There were isolated small amounts of dicamphor and dicamphoquinone, a substance melting at 156°C., and a larger quantity of an alkali-insoluble mixture.

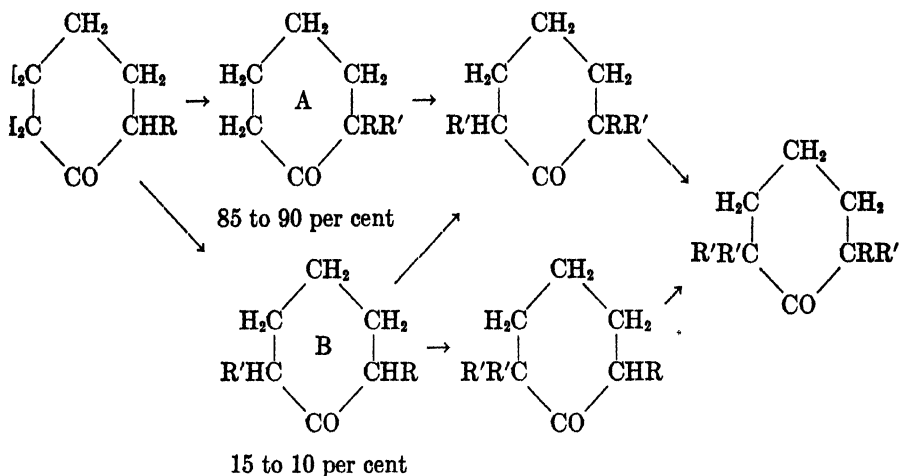
In the previous review, a number of articles by Cornubert and his co-workers (30, 31) were inadvertently overlooked, although the references were added on the proof (6, p. 178). These articles are now reviewed below.

### 1. The alkylation of cyclohexanone

The following scheme expresses the average results obtained in the alkylation of cyclohexanone itself with sodium amide and an alkyl halide in ethereal solution.



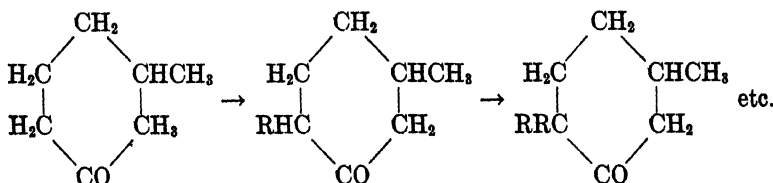
The fixation of one alkyl group is accompanied by that of a second alkyl group in smaller quantity. This reaction is the more important the more concentrated the solution of the ketone. At the same time, the importance of the condensation reaction increases (6, equation 56).

2. The alkylation of  $\alpha$ -substituted cyclohexanones

The percentage of the two isomers, A and B, depends to some extent upon the nature of the halogen in the alkyl halide, bromides and iodides giving the same yields, chlorides furnishing mixtures richer in ketone B. The alkyl group preëxisting in the  $\alpha$ -position does not always appear to have an influence on the phenomena of orientation. Phenylation and cyclohexylation of  $\alpha$ -methylcyclohexanone did not succeed. Isopropylation was effected with poor yield. Steric influences do not appear to have any definite effect.

3. Alkylation of  $\beta$ -methylcyclohexanone and of menthone

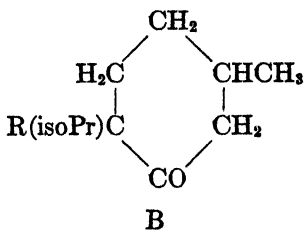
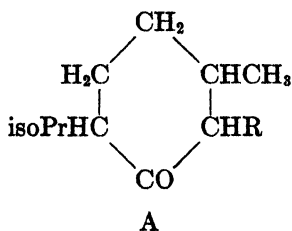
The alkylation of  $\beta$ -methylcyclohexanone proceeds for the most part in accordance with the following scheme, although minor amounts of the  $\alpha,\alpha'$ -dialkyl derivative are formed at the same time.



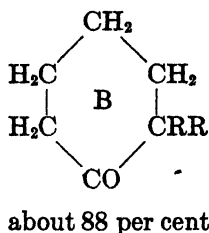
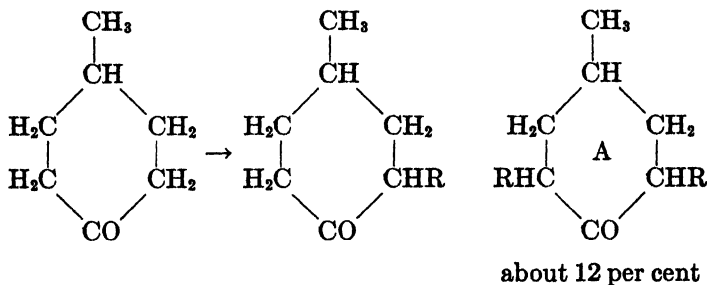
A  $\beta$ -alkyl group therefore has a manifest influence on the position taken by the entering alkyl groups.

Martine (6, p. 173) examined the methylation of menthone and erroneously concluded that the product was chiefly the symmetrical methyl-

menthone, formula A below. Cornubert and Humeau (31), however, conclude that the asymmetrical ketone (formula B) is the chief reaction product.



#### 4. The alkylation of $\gamma$ -methylcyclohexanone



Since the proportion of symmetrical and asymmetrical ketones, A and B, produced in the above reaction is about the same as when cyclohexanone itself is alkylated, the  $\gamma$ -methyl group has no influence on the phenomena of orientation.

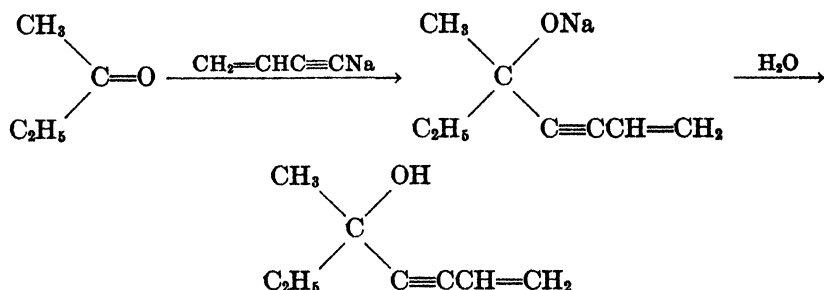
It is shown that the proportion of isomers formed in the alkylation of cyclohexanone or of the three monomethylcyclohexanones is not due to an effect of transposition, such as might be caused by the reagents used in the synthesis.

In the methylation of  $\alpha$ -methylcyclopentanone, Haller and Cornubert (6, p. 178) obtained a preponderance of the unsymmetrical  $\alpha, \alpha'$ -dimethylcyclopentanone, together with a smaller quantity of its  $\alpha, \alpha'$ -isomer.

In a later article, entitled "Contribution to a study of the extinction of the ketonic function," Cornubert and his coworkers (32) used sodium amide in preparing tetramethylcyclohexanone, tetraallylcyclohexanone, tetrabenzylcyclohexanone, methylisopropylallylcyclohexanone, and triallylmenthone. In the course of the work ketones were found which gave no bisulfite compound, oxime, or semicarbazone, although they could be reduced to the corresponding secondary alcohol.

*C'. The preparation of acetylenic carbinols*

Methyl ethyl ketone, vinylacetylene, ether, and sodium amide at temperatures of carbon dioxide snow give a 71 per cent yield of vinyl-ethynylmethyl ethylcarbinol, in accordance with the equation (15),



A patent has been issued for the preparation of the sodium salts of aliphatic ketones, to be used for making acetylenic carbinols (38).

Vinylethynylmethylcarbinol is made in 26 per cent yield by treating the sodium salt of vinylacetylene with acetaldehyde, but in the preparation of this and other secondary carbinols the results were not as good as in the preparation of the tertiary carbinols (15).

*D. The scission of ketones by means of sodium amide*

Two earlier papers of Haller and Bauer (64, 66) were overlooked in the first review, and are now abstracted.

Trialkylacetamides are prepared by heating trialkylacetophenones,  $\text{C}_6\text{H}_5\text{COCR}_3$ , in benzene or toluene with sodium amide (6, p. 124). Potassium hydroxide saponifies them with great difficulty, but the corresponding acids may readily be obtained by the action of nitrous acid upon them. There have been prepared the following acid amides, together with the corresponding acids: pivalamide (trimethylacetamide), dimethylethylacetamide, dimethylpropylacetamide, methyl-diethylacetamide, dimethylisopropylacetamide, methyl-diethylacetamide, triethylacetamide, methyl-ethylpropylacetamide, dimethyl-lauramide, benzyl-dimethylacetamide, and others.

Tribenzylmethane,  $(C_6H_5CH_2)_3CH$ , may be prepared by refluxing  $\omega, \omega, \omega$ -tribenzylacetophenone with sodium amide in xylene (73).

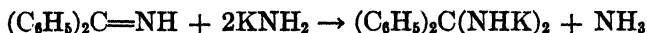
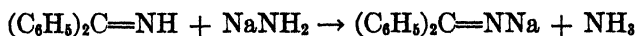
Bouveault and Levallois (12a) modified the method of Semmler (6, p. 127) for opening the ring of fenchone with sodium amide.

Chaix and de Rochebouet (16) heated fluorenone with sodium amide in toluene and obtained the amide of biphenyl-*o*-carboxylic acid.

Haller (60) heated tetramethyldibenzylacetone with sodium amide for three days in xylene, obtaining isobutylbenzene and the acid amide,  $C_6H_5CH_2C(CH_3)_2CONH_2$ . Similarly,  $C_6H_5CH_2CH_2COC_2H_5$  gives on alkylation 1-phenyl-2,2,4,4-tetramethyl-3-pentanone, which is decomposed into isobutylbenzene and the amide of trimethylacetic acid. Haller and Bauer heated hexamethylacetone, pentamethylethylacetone, tetramethyldiethylacetone, and triethylpinacolone with sodium amide, obtaining hydrocarbons and trisubstituted acetamides (67a).

### G. Ketimines

Benzophenoneimine reacts with sodium amide to form a salt, and with potassium amide to form the salt of an addition compound, in the manner of the following equations (138):



## XII. ACIDS AND THEIR DERIVATIVES, EXCLUSIVE OF ESTERS

### A. Acids<sup>3</sup>

Wood and Bergstrom (156) have recorded their inability to prepare a dipotassium salt of formic acid ( $K \cdot COOK$  or  $C(OK)_2$ ) by treating this acid with an excess of potassium amide in liquid ammonia.

### B. Acid amides and proteins

The work of Miss Fulton concerning the formation of salts of the acid amides and their decomposition into hydrocarbons by heating with an excess of the reagent has now been published (47a; 6, p. 132). Freer and Sherman (48) previously prepared the sodium salts of formamide and acetamide with the use of sodium amide.

### C. The indigo synthesis

Indigo is formed by heating phenylglycinesulfocarboxylic acid with sodium amide at 220°C. (84).  $\alpha$ -Phenylhydantoin and its homologues react with heated alkali amides, or with a mixture containing the alkali

<sup>3</sup> See also section VIII A.

hydroxides in addition, to form a substance (probably indoxyl) which gives indigo on oxidation in air (39).

Belart (3a) has modified the customary process for the production of indigo (6, p. 134) by using organic derivatives of sodium amide in place of sodium amide itself, to cyclize phenylglycine-*o*-carboxylic acid. The sodium derivatives of aniline, naphthylamine, diphenylamine, tolylamine, and xylylamine have been specifically mentioned.

#### *D. The preparation of substituted indoles*

Julian and Pikel (81) used the method of Verley and Beduwé (150) to prepare *n*-propylindole.

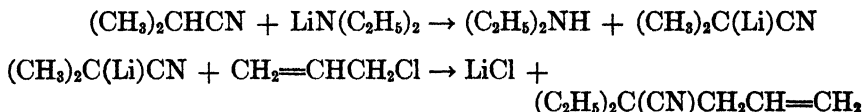
#### *E. Acid chlorides*

Carbonyl chloride has been treated previously (see pp. 422, 431) (118, 119).

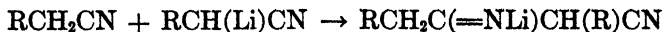
#### *F. Nitriles and related compounds*

##### 1. The alkylation of nitriles

Ziegler and Ohlinger (167; 6, pp. 136-7) found that secondary aliphatic nitriles react with lithium diethylamide and similar metallic alcoholates of the ammonia system to form salts which could be alkylated, as shown by the following equations:



In attempting to extend this reaction to the preparation of salts of the primary nitriles, such as acetonitrile, it was found that large amounts of the lithium derivatives of the dimeric nitriles were formed, particularly if the ratio of nitrile to lithium dialkylamide were 2 to 1.



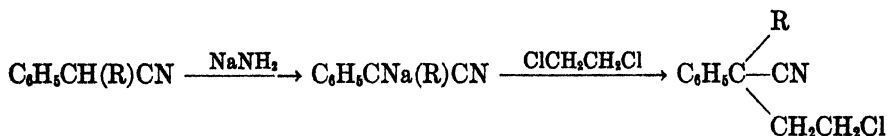
The reaction is analogous to the formation of ketimides when nitriles are treated with the Grignard reagent. As an example, acetonitrile, added to a solution of lithium diethylamide in ether at  $-10^\circ\text{C}$ ., gives a 78 per cent yield of the dimeric nitrile. Similarly, *n*-butyronitrile gives 71.5 per cent of the dimer,  $\alpha$ -butyrylbutyronitrile, but a 90 per cent yield is obtained when lithium ethylanilide is used as the condensing agent (166).

Many patents have been issued to Ziegler for the preparation of substituted nitriles, and their conversion to acid amides of possible medicinal value (162). One such patent (162b) states that secondary nitriles of the



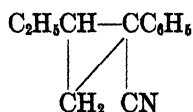
general formula,  $R_2CHCN$ , in which R represents alkyl (except vinyl) or aralkyl groups, are treated with alkali metal, magnesium, or halogen magnesium substitution products of secondary aliphatic or hydroaromatic amides to form metal derivatives, these then being treated with halogen alkylene compounds or with dialkyl sulfates. Thus, diallylacetonitrile is treated with dicyclohexylamine and  $(C_2H_4Br)_2Mg$  solution ( $\rightarrow (C_6H_{11})_2NMgBr$ ), a  $-MgBr$  derivative of the nitrile being formed. The  $-MgBr$  group is replaced by allyl on treatment with allyl bromide, to give triallylacetonitrile.

Hastings and Cloke (71) prepared several  $\alpha$ -phenyl- $\alpha$ -alkyl- $\gamma$ -chlorobutyronitriles by the method of Bodroux and Taboury (6, pp. 138-40), and as shown by the following equations ( $R = \text{alkyl}$ ):

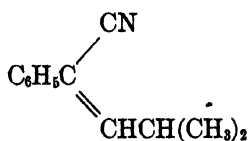


Ethylene chlorohydrin can be used in this synthesis, the hydroxyl group of the resulting condensation product being replaced with chlorine, but the method represented by the equation is recommended. The alkylphenylbutyronitriles form pyrrolines by the method of Cloke (25a).

Murray and Cloke (111a) record the preparation of 1-phenyl-2-ethylcyclopropanecarbonitrile (A),  $\alpha$ -phenyl- $\beta$ -ethylacrylonitrile,  $\alpha$ -phenyl- $\beta$ -isopropylacrylonitrile (B), and some of their derivatives by the general method of a previous article (cf. 6, p. 140).

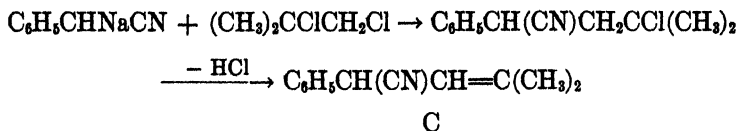


A



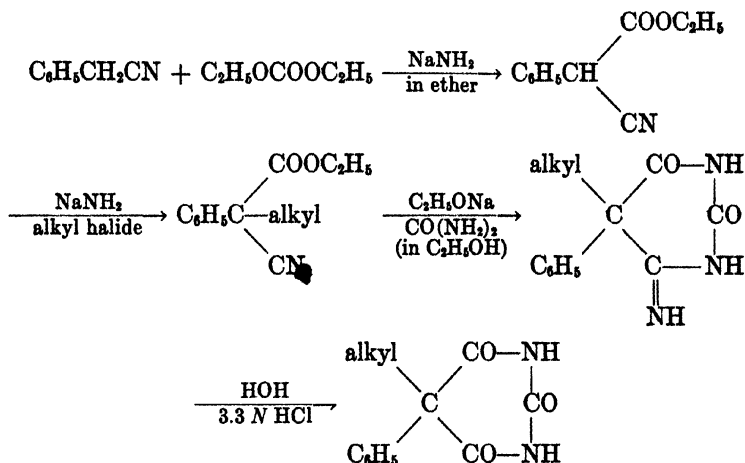
B

The formation of B by the condensation of 1,2-dichloroisobutane and phenylacetonitrile with sodium amide involves a rearrangement, possibly from the  $\beta, \gamma$ -unsaturated nitrile (C), which would result from the reaction,



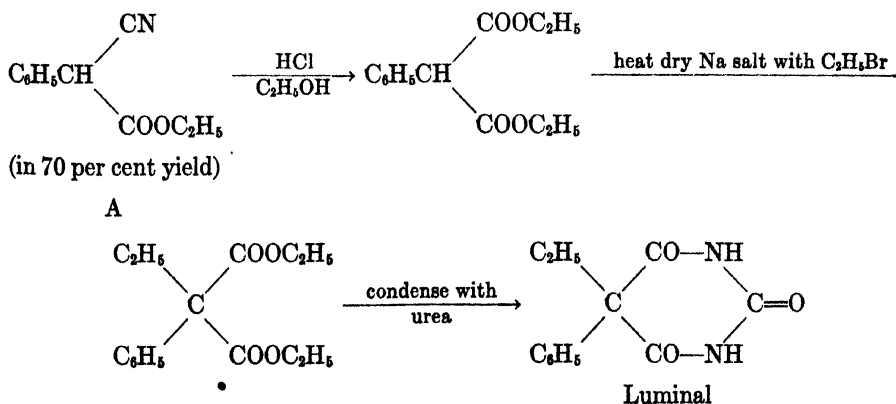
Chamberlain, Chap, Doyle, and Spaulding (17) have prepared the following 5,5-alkylphenylbarbituric acids from intermediates made with the

use of sodium amide: ethyl-, isopropyl-, isoamyl-, *n*-hexyl-, and *n*-heptyl. A typical reaction is expressed by the following equations:



It was noted that the condensation of phenylacetone nitrile with diethyl carbonate is best effected by using sodium amide in absolutely anhydrous ether, with continued refluxing and stirring. A by-product results from the probable reaction of two moles of the nitrile with one of the carbonate, its formation being favored by non-anhydrous conditions and too long refluxing. Alkylation of the cyanophenylacetate and the condensation of the resulting compound with urea takes place in absolute alcohol in the presence of sodium amide or sodium ethylate, the product, a 5,5-alkyl-phenyl-4-iminobarbituric acid being hydrolyzed to a 5,5-alkylphenyl-barbituric acid.

Nelson and Cretcher (114) had previously used the method just described to prepare ethyl phenylcyanoacetate (A), which was converted to luminal in accordance with the scheme,



Phenylvinylloxyethylacetonitrile,  $C_6H_5CH(CH_2CH_2OCH=CH_2)CN$ , was prepared from phenylacetonitrile,  $\beta$ -chloroethyl vinyl ether, and sodium amide.

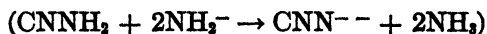
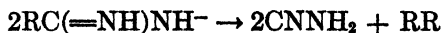
Kaufmann, Dändliker, and Burkhardt (86) made the sodium salt of phenylacetonitrile in ether with the use of sodium amide, and then added ethyl quinaldate, obtaining cyanobenzyl quinolyl ketone,  $C_6H_5NCOCH(CN)C_6H_5$ . When this is saponified (with sulfuric acid) an acid is formed, which loses carbon dioxide, giving benzyl 2-quinolyl ketone.

$\gamma$ -Chlorobutyronitrile and sodium amide react to give cyclopropane-carboxylic acid amide in poor yield (100).

Dolique (35a) prepared  $\alpha$ -phenylhexonitrile from phenylacetonitrile, sodium amide, and *n*-butyl bromide.

## 2. The formation of salts of the amidines

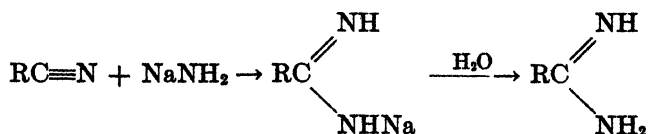
Concentrated solutions of the potassium salts of the lower aliphatic acid amidines in liquid ammonia conduct the current readily, and at high current densities give a mixture of saturated hydrocarbon gases at the anode (50). Salts of the amidines are of course readily prepared by adding a nitrile to a solution of potassium amide in liquid ammonia (29). Only in the case of acetamidine did the anodic reaction go in the anticipated manner, that is, in the sense of the equation,



In all other cases, the hydrocarbons obtained were chiefly mixtures of methane and ethane, which presumably resulted from some kind of thermal decomposition at the electrode. Insofar as the formation of ethane and the ammonocarbonic acid, cyanamide (as a potassium salt), is concerned, this reaction is analogous to the well-known Kolbe synthesis, in which ethane and an aquocarbonic acid salt (potassium carbonate) are formed anodically when a concentrated aqueous solution of potassium acetate is electrolyzed.

Ziegler (164) has patented the preparation of acid amidines containing at least four carbon atoms by treating the nitrile with sodium amide (in the absence of liquid ammonia) at a temperature below the decomposition temperature of the resulting sodium salt of the amidine. The latter is formed on hydrolysis.

Kirssanov and Poliakova (89) studied the action of sodium amide on aromatic nitriles, and found that unsubstituted amidines were always obtained, in accordance with the equation,



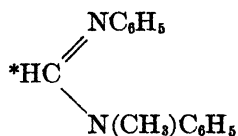
Only small yields of amidine were obtained by heating the aryl cyanide with sodium amide alone, but in the presence of a diluent (boiling toluene, six hours) the following yields have been obtained: benzamidine from benzonitrile, 15 to 20 per cent; *p*-toluamidine from *p*-tolunitrile, 60 per cent; and  $\beta$ -naphthoamidine from  $\beta$ -naphthonitrile, 40 to 50 per cent.

The action of sodium amide on nitriles and on Schiff bases is similar, since in the first stage the reagent always adds to a multiple bond between carbon and nitrogen.

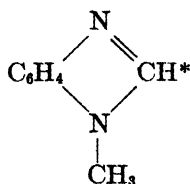
Acetonitrile reacts violently with an excess of sodium amide in ether, but in spite of numerous variations in the conditions under which the reaction was carried out, it was impossible to isolate acetamidine. The velocity of polymerization (dimerization, probably) appears to be more rapid than the velocity of formation of the amidine.

The claim is made that the crystalline compounds obtained by Cornell (29) when metallic amides in liquid ammonia react with nitriles are probably not the salts of amidines, but are double compounds of the nitriles with the amidines. Cornell's analyses, however, seem to indicate quite definitely that salts of the type,  $\text{RC}(=\text{NH})\text{NHM}$ , are formed (M is a univalent metal).

Diphenylmethylformamidine



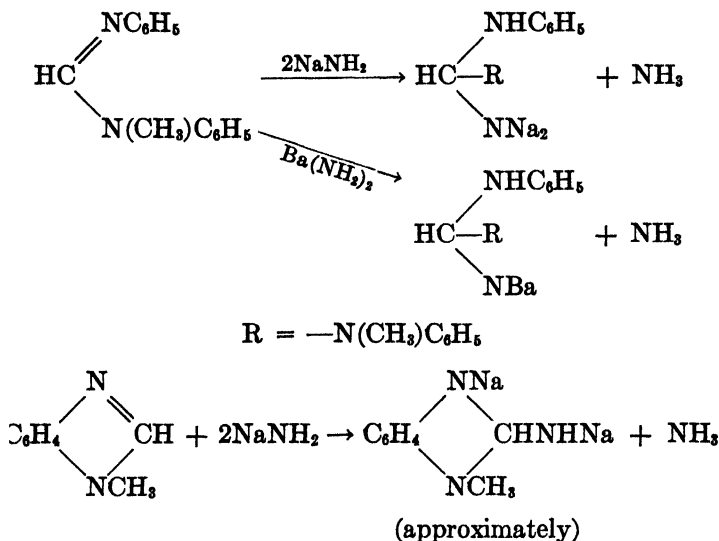
and *N*-methylbenzimidazole



may be regarded as substituted amidines, and therefore as related to the nitriles, or as neutral esters of ammonioformic acid, or formamidine. Unsuccessful attempts were made by Wood (156) to show that the hydrogen atoms designated by asterisks were acidic and capable of replacement

with an alkali metal. Such metallic salts it was hoped would clearly show the reactions of compounds containing "divalent" carbon.

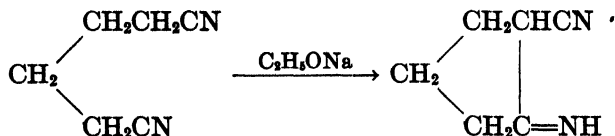
However, it was found that both alkali and alkaline-earth amides added to the double bond between carbon and nitrogen to give substances that might be regarded as salts of ammonoöorthoformic esters. Thus,



The assumed structure of these salts has not been definitely proven.

### 3. The use of aliphatic dinitriles in the preparation of large-ring systems

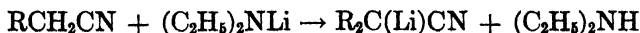
Thorpe (145), in 1909, treated adiponitrile with sodium ethylate and obtained 1-imino-2-cyanocyclopentane, in accordance with the equation:



The synthesis of larger rings by this process always gave unsatisfactory yields, until Ziegler, Eberle, and Ohlinger (166) discovered that metallic derivatives of the primary and secondary alkyl or aralkyl amines were excellent condensing agents. Unfortunately, their use involves several experimental difficulties. The tendency of a dinitrile to dimerize, in the manner of the equation,



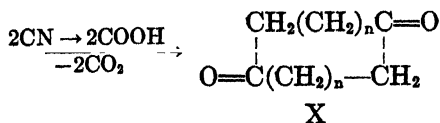
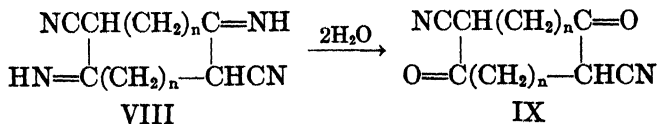
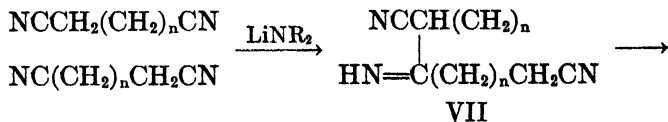
must be overcome, and the formation of a dilithium (or dimetallic) salt of a nitrile must be prevented, since it is only the monolithium salt that readily undergoes cyclization. (Reactions of the type,



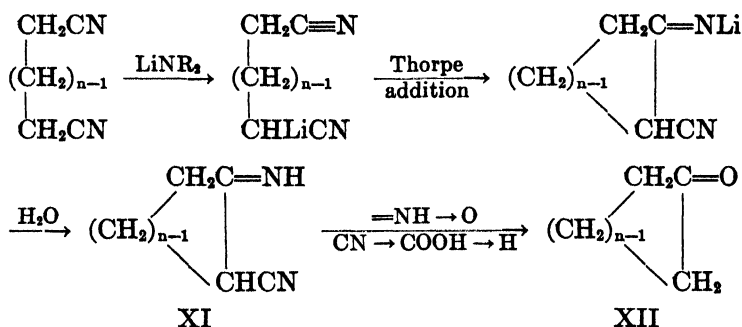
are practically irreversible under the conditions used.) The reaction of dinitriles with substituted alkali metal amides to give five- and six-membered ring compounds occurs readily in spite of fairly high concentrations of the condensing agent, but the larger rings can be made only by adding the nitrile very slowly to a solution of the condensing agent in a large volume of ether, in order to keep the nitrile concentration below the point at which unwanted side reactions predominate. The following examples will illustrate:

(1) An ethereal solution of lithium diethylamide,  $(C_2H_5)_2NLi$ , (0.8 *N*) was added to sebacic dinitrile,  $CN(CH_2)_8CN$ , in the same solvent, a 13 per cent yield of cyanocycloheptanone being isolated after hydrolysis. (The imino group in the primary product has been replaced by oxygen.)

(2) The following procedure gave much better results: 1,14-Dicyanotetradecane (50 g.) was added with stirring to a solution of lithium phenylethylamide (from 93 g. of ethylaniline and an equivalent of lithium *n*-butyl) in 3 liters of ether during  $14 \times 24$  hours. On standing the ethereal solution deposited 7 g. of a diketimide (formula VIII,  $n = 13$ , a 30-membered ring). After evaporation of the solvent ether there was obtained a residue (34 g.), from the hydrolysate of which cyclopentadecanone (16.6 g., or a yield of 37 per cent) and a diketone (thirty carbon atoms in the ring) were isolated. Some of the reactions that occur in this synthesis are expressed in generalized terms below.



and



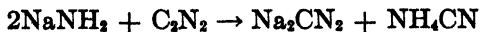
(3) From 55 g. of 1,16-dicyanohexadecane, under the conditions of the above experiment, there were obtained 26 g. of dihydrocivetone (formula XII,  $n = 15$ ) and 9 g. of tetratriacontadione (formula X,  $n = 15$ ), among other products. The total yield of cyclic materials was 70 per cent of the theoretical.

Since this article was published, there have appeared a large number of patents dealing with the preparation of cyclic compounds containing large rings, essentially by the methods outlined above, but with some modifications (163). The following is representative (163a): Nitriles having the general formula,  $\text{NC}(\text{CH}_2)_n\text{CN}$ , can be condensed to form cyclic  $\alpha$ -cyano-ketimides having the formula,  $\text{HN}=\text{C}(\text{CH}_2)_{n-1}\text{CHCN}$ , by acting upon them with a condensing agent of the type  $(\text{R}'\text{R}''\text{N})\text{M}$ , where  $\text{R}'$  and  $\text{R}''$  may be alkyl, aralkyl, aryl, or alicyclic radicals, while  $\text{M}$  may be an alkali metal, such as sodium or lithium, an alkaline-earth metal, as magnesium, or other metals, such as aluminum or the rare earths. At the same time, two moles will combine to form cyclic diimine dinitriles.

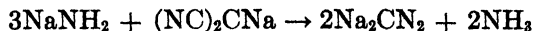
In the case of cyclic systems comprising five or six links, the reaction occurs smoothly without any particular degree of dilution being required. When preparing cyclic compounds containing more than six links, it has been found preferable to operate with a high degree of dilution. Operation at low concentrations is important when producing cyclic systems composed of more than seven links. By saponification, the  $\alpha$ -cyano-ketimines can be converted to  $\alpha$ -cyanoketones. These compounds may be used in organic syntheses, or for the preparation of scents.

#### 4. Cyanogen

Perret and Perrot (118) have examined the action of sodium amide on cyanogen, and find that the first reaction is expressed by the equation (cf. 29),



That is to say, an anammonide of an ammonoöxalic acid is split by an ammono base, sodium amide, to salts of an ammonocarbonic and an ammonocarbonous acid. (It is assumed that ammonium cyanide will react further with sodium amide to form sodium cyanide and ammonia.) Dicyanimide,  $(\text{NC})_2\text{NH}$ , is not formed, since it reacts with sodium amide in the following manner:

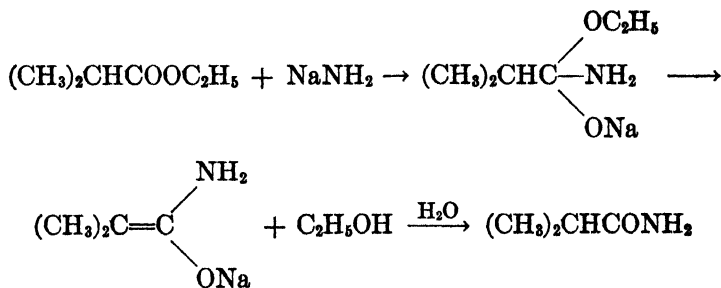


Franklin (47b) has previously found that all ammonocarbonic acids—including, of course, dicyanimide—react with heated sodium amide to give disodium cyanamide,  $\text{Na}_2\text{CN}_2$ .

### XIII. ESTERS<sup>4</sup>

Wood (156) records the failure to prepare potassium ethyl carbonite,  $\text{C}(\text{OC}_2\text{H}_5)\text{OK}$ , by treating ethyl formate with potassium amide in liquid ammonia. The ester appears merely to be saponified.

Ethyl chloroformate, added to the product of the reaction of sodium amide and ethyl isobutyrate in ether, gives a mixture from whose hydrolysate may be isolated unused ethyl isobutyrate, ethyl carbonate, isobutyramide (the chief product), and diisobutyramide. Certainly the last two would be obtained even in the absence of ethyl chloroformate. The following interpretation is given.



Sodium amide is inferior to sodium ethylate as a condensing agent in the reaction of diethyl malonic ester and urea to form diethylbarbituric acid (45).

Tingle and Gorsline (146) claim that sodium amide is almost useless in effecting Claisen condensations with camphor as the ketone.

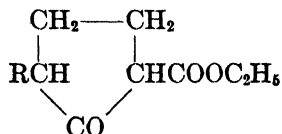
Diethyl terephthalate and acetone are condensed by sodium amide in ether to terephthalaldiacetone (3b). Lux (102) finds that sodium amide in ether effects a condensation between ethyl carbonate and acetone to

<sup>4</sup> See also section XII, p. 455, concerning *N*-methylbenzimidazole and diphenylmethylformamidine.



form acetoacetic ester, the yield (30 per cent), however, being inferior to experiments in which metallic sodium was used (38 to 41 per cent).

Haller and Cornubert (69a) have improved the method of Bouveault and Locquin (6, p. 147) for the preparation of ethyl cyclopentanone-carboxylate,



(yield, 70 to 80 per cent) by cyclization of ethyl adipate,  $\text{C}_2\text{H}_5\text{OCO}(\text{CH}_2)_4\text{COOC}_2\text{H}_5$ , with sodium amide. This is a Dieckmann reaction. ( $\text{R} = \text{H}$ .) The corresponding  $\alpha$ -methyl derivative ( $\text{R} = \text{CH}_3$ ) was made from ethyl  $\alpha$ -methyladipate.

The work of Griswold (6, p. 146) concerning the action of potassium amide in liquid ammonia on the dialkylcyanamides (i.e., esters of an ammonocarbonic acid, cyanamide) has been published since the first review (47).

Diethoxyacetic ester,  $(\text{C}_2\text{H}_5\text{O})_2\text{CHCOOC}_2\text{H}_5$ , and sodium amide react in ether to give the sodium salt of diethoxyacetamide (129) (saponification).

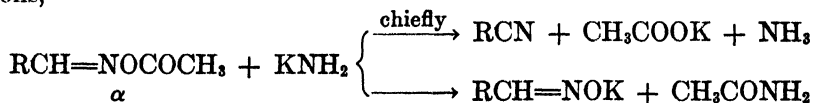
Schwarz and Giese (135) state that ethyl and amyl nitrites fail to react with liquid ammonia at low temperatures, although a vigorous reaction occurs with a solution of potassium amide, in the manner, essentially, of the equation,



#### XIV. ORGANIC DERIVATIVES OF HYDROXYLAMINE AND HYDRAZINE

Kraus and Bien (90) prepared disodium benzhydrazide,  $\text{C}_6\text{H}_5\text{NNa} \cdot \text{NNaC}_6\text{H}_5$ , for conductivity work by treating hydrazobenzene with sodium amide in liquid ammonia, but they were unable to make the monosodium salt.

Hauser and Jordan (72), in connection with an investigation of the action of alkalis on acetyl- $\alpha$ - and  $\beta$ -benzaldoximes have found that the former are converted to potassium salts of the oxime and acetamide, or to nitriles, potassium acetate, and ammonia, in accordance with the equations,

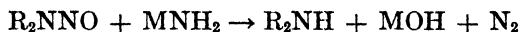


$\text{R}$  is a substituted phenyl group. When  $\text{R}$  is 4-methoxyphenyl, 47 per cent of the theoretical quantity of the nitrile, a trace of acetic acid, and 43 per

cent of the oxime are formed; when R is 2-chlorophenyl, the yields are 80 per cent of the nitrile and 9 per cent of the oxime; and when R is 3-nitrophenyl, there is obtained 23 per cent of the nitrile, 60 per cent of a gum, and 8 per cent of the oxime. From this, and other work not reported here, it is concluded that  $\alpha$ - and  $\beta$ -aldoxime acetates undergo fundamentally the same type of reaction with alkali, but differ primarily in the ease with which they eliminate acetic acid, the  $\beta$ -isomers undergoing this reaction more readily.

#### XV. NITRO AND NITROSO COMPOUNDS

Diphenylnitrosamine in liquid ammonia solution reacts with the amides of lithium, sodium, potassium, and calcium in accordance with the equation,



For simplicity, M is an univalent alkali metal.

*p*-Tolynitrosamine reacts similarly with sodium amide and potassium amide, but dibenzylnitrosamine and methylphenylnitrosamine do not react in the manner of the above equation. In these reactions no direct evidence was found for the formation of the salt,  $NO \cdot NHK$  (44).

Buehler (14), in continuing the preliminary work of Williams and Bergstrom (6, pp. 151-2), has found that nitrobenzene reacts with sodium amide in liquid ammonia ( $-33^\circ C.$ ) with the evolution of some nitrogen. There is practically no further formation of gas after standing for half a day, indicating that the dissolved substance has a fair stability. If  $\beta$ -naphthol is added at this stage, or if the initial reaction is carried out in the presence of  $\beta$ -naphthol, there results the dye, phenylazo- $\beta$ -naphthol,  $C_6H_5N=NC_{10}H_6OH-\beta$ . The yields depend upon experimental conditions and are as high as 33 per cent. Sodium amide must be in excess of two equivalents for the best results. Dye formation was observed when the following nitro compounds were treated with sodium amide in the presence of  $\beta$ -naphthol: *p*-nitrotoluene, 4-nitrobiphenyl, *o*-nitrobenzoic acid, *o*-nitrotoluene, and 4,4'-dinitrobiphenyl. The above reactions, whose significance will be discussed later, follow the equation,

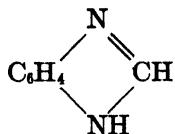


A

Compound A must be sodium normal benzene diazotate, since the isodiazotate does not couple with  $\beta$ -naphthol in ammonia.

XVI. FIVE-MEMBERED HETEROCYCLIC RING SYSTEMS<sup>5</sup>

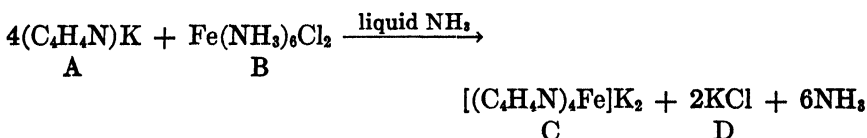
With the use of the metallic amides, only one hydrogen atom of benzimidazole,



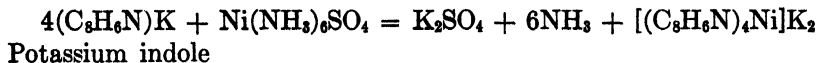
can be replaced by potassium, lithium, or barium in liquid ammonia, in agreement with the accepted formula above. (The lithium and barium salts retain ammonia of crystallization.) It has thus proven impossible to prepare nitrogen analogues of the hypothetical dipotassium aquocarbonite,  $\text{C}(\text{OK})_2$  (156).

Sodium indole may be prepared by introducing sodium amide into molten indole at 120–160°C. (153).

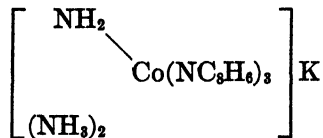
Schmitz-Dumont and St. Pateras (134a) have prepared several coordination compounds of potassium pyrrole and potassium indole in liquid ammonia, in the general manner represented by the equations,



Potassium pyrrole (A) is very soluble in liquid ammonia, as is the coordination compound (C), while B and D have very low solubilities.



A double salt of the composition,



is formed from potassium indole and chloropentamminochromium chloride in liquid ammonia. A more complex salt of this nature was prepared from potassium indole and hexamminocobaltic chloride.

$\gamma$ -Butyrolactone does not react with sodium amide in ether (107a).

<sup>5</sup> The reaction of *N*-methylbenzimidazole with the alkali and alkaline-earth amides is described under section XII F.

2-Methylfurane does not react with sodium amide at temperatures between 60°C. and 100°C. (53).

## XVII. SIX-MEMBERED HETEROCYCLIC RING SYSTEMS

### A. Pyridine and its derivatives

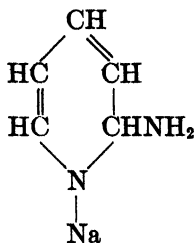
According to Goost and Lommel (55), pyridine and its homologues are refined by treatment with a compound containing the group  $\text{=N}\cdot\text{M}$  or  $\text{—N}\cdot\text{M}$ , where M is an alkali or alkaline-earth metal. Thus, commercial pyridine may be heated to 110°C. with 5 per cent of disodium cyanamide,  $\text{Na}_2\text{CN}_2$ , or stirred at ordinary temperature with 3 to 5 per cent of sodium amide. This treatment is particularly useful, it is claimed, as a preliminary to catalytic hydrogenations.

The synthesis of 2-aminopyridine, by the action of sodium amide on pyridine in heated indifferent solvents, has been known since the work of Chichibabin and Seide in 1914 (25), but has since been the subject of occasional patents. Thus, an 80 per cent yield is claimed in a German patent (35), if equimolar proportions of sodium amide and pyridine are brought into reaction in a medium such as toluene, at temperatures that are preferably under 100°C. It has been the experience of many that a yield of 50 to 60 per cent is all that can be expected (cf. 154). Shreve (136) has used a steel ball mill for the preparation of sodium amide, and for a reaction vessel in which the synthesis of 2-aminopyridine and 2,6-diaminopyridine is carried out. 2-Aminopyridine, 2,6-diaminopyridine, and 2,4-diaminopyridine have been obtained by heating a suspension of sodium amide in dimethylaniline with pyridine (116). With sodium amide 2-aminopyridine forms a sodium salt, which can be alkylated with methyl iodide (24).

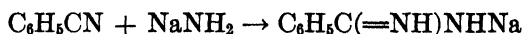
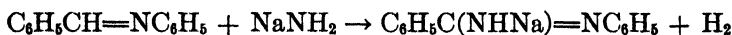
Chichibabin (20) has prepared 2,6-dimethyl-4-aminopyridine by heating 2,6-dimethylpyridine with sodium amide in toluene for twenty-two hours. A German patent (19) relates to the preparation of aminated pyridine homologues in the presence of high-boiling indifferent solvents (xylene, cumene, mesitylene, etc.) at temperatures over 150°C., using either sodium amide or metallic sodium and gaseous ammonia. 6-Amino-2-methyl-5-ethylpyridine and 2-amino-4-ethylpyridine have been described, among others. Schneiderwirth (133) has heated a mixture of 2-alkylpyridine with sodium amide to a temperature of not less than 200°C., obtaining 4,6-diamino-2-alkylpyridines, such as 4,6-diamino-2-methylpyridine and 4,6-diamino-2-propylpyridine.

Feist and coworkers (43) prepared 2-aminopyridine by a modified Chichibabin method, which is claimed to be an improvement. The mechanism of the formation of 2-aminopyridine has been extensively dis-

cussed by Kirssanov and Ivastchenko (88) and by Kirssanov and Poliakova (89) (see section X), who conclude that an addition compound,

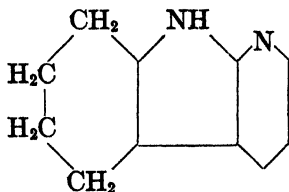


is the first reaction product, in accordance with an earlier suggestion of Ziegler and Zeiser (168). On heating this loses sodium hydride to give 2-aminopyridine, which is subsequently converted by the liberated sodium hydride to a sodium salt. Support for this view was obtained as a result of the study of reactions of the type,



The mechanism of this reaction has also been discussed by Kabachnik (82), who likewise favors Ziegler's scheme (168) for the formation of 2-aminopyridine. Dipyrityls accompany amino derivatives in all cases, and sometimes predominate in the more complex compounds, as is the case with 2,5-dimethylpyrazine (6, p. 161). Their formation is due to the replacement of an  $\alpha$ - or  $\gamma$ -hydrogen of the pyridine base with sodium, ammonia being evolved. The sodium compound then adds to the double bond between carbon and nitrogen of another molecule of the heterocyclic base, just as does sodium amide, to give a dihydro derivative, which is oxidized to the dipyrityl.

2-Aminopyridine condenses with *o*-chlorocyclohexanone and sodium amide in toluene (78) to

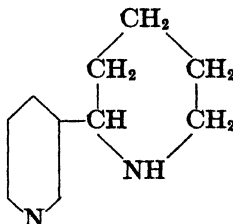


3-Hydroxypyridine in methanol and sodium amide in *p*-cymene when heated together give 2,6-diaminopyridine, the hydroxyl having been replaced by hydrogen (121).

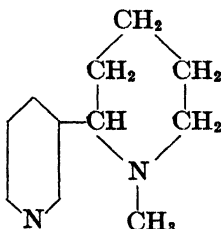
Tjeen Willink, Jr., and Wibaut (147) find that 2,2'-dipyrityl is only

slightly attacked by sodium amide in boiling toluene (fourteen hours) with the apparent formation of a small amount of a diaminodipyridyl, m.p. 185–6°C. (Boiling xylene gives better results.) 2,2'-Diamino-4,4'-dipyridyl may be formed more readily (19). A monoamino-2,2'-dipyridyl may be prepared by treating 2,2'-dipyridyl with an excess of potassium amide and potassium nitrate in liquid ammonia at room temperatures (m.p. of product, 135.5–6.5°C.) (7a).

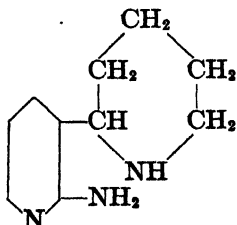
Several articles (83, 85, 106) have appeared dealing with the amination of anabasine,



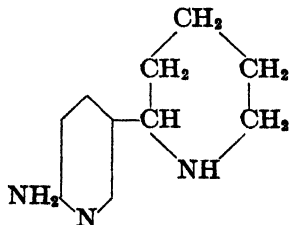
and *N*-methylanabasine,



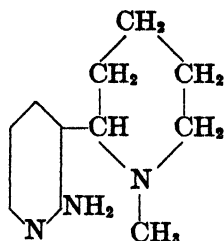
The reactions were best carried out with sodium amide in dimethylaniline at a temperature of 120–150°C., since yields of about 40 per cent were obtained, as against the 5 per cent yield reported by Menschikov, Grigorovitch, and Orechhoff (106) in boiling xylene. *N*-methylanabasine was however aminated in this solvent to two isomeric amino-*N*-methylanabasines, which are formed in a total yield of 45 to 50 per cent (106). The following compounds have been prepared:



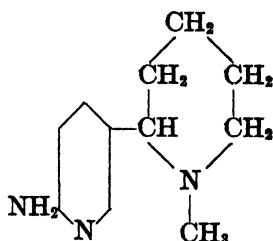
$\alpha$ -Aminoanabasine  
m.p. 89.5–90°C.



$\alpha'$ -Aminoanabasine  
m.p. 109°C.

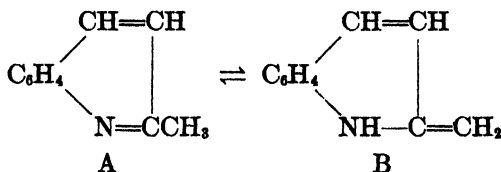


$\alpha$ -Amino-*N*-methylanabesine  
m.p. 95°C.

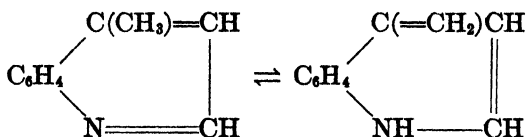


$\alpha'$ -Amino-*N*-methylanabesine  
oil

Some years ago, Chichibabin (21) suggested that the 2- and 4-methylpyridines and the 2- and 4-methylquinolines were tautomeric in the sense,



and



That is to say, the group  $\text{CH}_3\text{C}=\text{N}-$  is tautomeric with  $\text{CH}_2=\text{C}-\text{NH}-$ . In lepidine (4-methylquinoline, formula above) and in 4-methylpyridine the methyl is separated from the  $=\text{C}=\text{N}-$  by the  $(-\text{CH}=\text{CH}-)$  group, and so behaves in the same manner as quinaldine (cf. 50a).

The tautomerism of quinaldine was discussed in an earlier article by one of us (3c) from the standpoint of the ammonia system, and it was seen that A and B (see formulas above) are related to one another as the keto modification is to its corresponding enol. (Chichibabin's article was referred to rather inadequately in reference 3c, although a statement to the contrary was made in reference 22.) Alkali amides convert quinaldine in liquid ammonia to very soluble, red, metallic salts, in which the metal, or rather the anionic charge, is located either on the side-chain carbon or on the nitrogen. (Ziegler and Zeiser (169) prefer the first formula.) 2-Alkylquinolines may readily be obtained by alkylating the potassium or sodium salts of quinaldine in liquid ammonia (3c) or the lithium salt in ether (169).

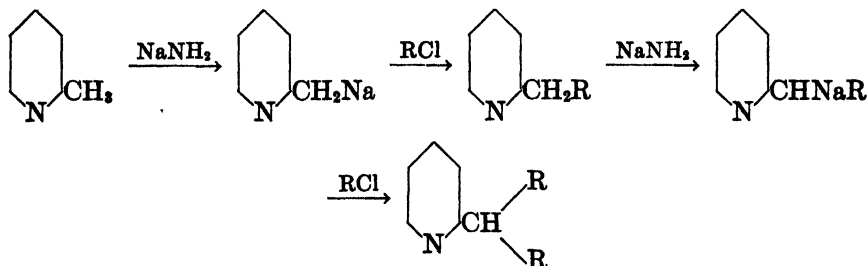
In 1914, Chichibabin and Seide (25) reported unsuccessful attempts to

alkylate 2-methylpyridine by treating it simultaneously with sodium amide and methyl iodide, but, unfortunately, the Russian original was not available to us, and the abstracts did not mention it. In one experiment with ethyl iodide, sodium amide, and 2-methylpyridine, diethylamino-2-picoline was obtained, together with a small quantity of a base having the composition of a diethylaminopropylpyridine, but the work was not described until later (22).

Recently, Chichibabin has again taken up the question of alkylation of  $\alpha$ - and  $\gamma$ -alkylquinolines and pyridines (22, 23). The reactions were usually carried out at room temperatures or slightly above with sodium amide, a 2- or 4-alkylpyridine or quinoline, or a 2,6-dialkylpyridine and an alkyl halide. The following directions are typical: The pyridine base is mixed in a round-bottom flask (reflux condenser) with an excess of finely pulverized sodium amide (which must be of very good quality). The liquid becomes colored yellow, then brown, or even brown-violet. The alkyl halide is added in small portions at a time, usually with cooling. With  $\gamma$ -picoline and quinaldine, it is necessary to cool during the entire reaction period. In some cases a little dry ether is added. The pyridine or quinoline base is usually in excess. The product is worked up after the mixture has stood overnight. The yield of alkylated products, if alkyl chlorides are used, is not inferior to 40 per cent, and is usually 50 to 60 per cent of the monosubstitution product, or 70 to 80 per cent, if disubstitution products are included.

The ease of formation of metallic derivatives varies strongly with different pyridine bases.  $\gamma$ -Picoline reacts much more readily than  $\alpha$ -picoline;  $\beta$ -collidine ( $\gamma$ -methyl- $\beta$ -ethylpyridine) differs little from  $\alpha$ -picoline. 2,6-Dimethylpyridine is even less reactive than  $\alpha$ -picoline.

The alkyl bromides and iodides, the latter in particular, are less satisfactory than the chlorides in this synthesis. The two principal reactions may be expressed by the representative equation below,



Among the compounds prepared are the following: 2-( $\omega$ -phenylethyl)-pyridine, 2-(dibenzylmethyl)pyridine,  $\gamma$ -phenylpropylpyridine, 2-*n*-amylpyridine, 2-isoamylpyridine, 2-cyclohexylmethylpyridine (hexahydro-



benzylpyridine), 2-butenylpyridine (from sodium amide, allyl chloride, and 2-methylpyridine), 2-propylpyridine, 4-phenylethylpyridine, 4-isobutylpyridine, diisopropylpicoline, 4-*n*-amylpyridine, 4-(di-*n*-butylmethyl)pyridine, 4-isoamylpyridine, 4-(diisobutylmethyl)pyridine, 4-propylquinoline (from lepidine, sodium amide, and ethyl iodide in 90 per cent yield), monobenzylquinaldine (65 per cent yield), and dibenzylquinaldine (25 per cent yield), the last two in the same reaction.

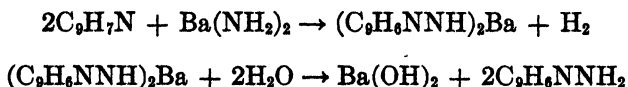
*B. Quinoline, isoquinoline, and their derivatives<sup>6</sup>*

In the previous review it was recorded that potassium amide and sodium amide react with quinoline in liquid ammonia at room temperatures to form resins, with occasional traces of 2-aminoquinoline (6, p. 158). It has now been found (7a) that the latter may be prepared in 50 to 55 per cent yield if the reaction is carried out in the presence of potassium nitrate, which is reduced to potassium nitrite in the process. The essential reaction is therefore the following:



A 10 per cent yield of 4-aminoquinoline was also obtained in one experiment. An excess of a soluble amide ( $\text{KNH}_2$ ) is necessary.

The reaction between barium amide and quinoline in liquid ammonia at room temperatures leads to the formation of both 2-aminoquinoline and hydrogen in good yields, in accordance with the equation (4),



The reaction occurs irrespective of the relative amounts of barium amide and quinoline. Barium ion appears to catalyze the reaction, which is greatly accelerated by ammonia-soluble barium salts such as the thiocyanate. Strontium amide is less effective than barium amide in the above, while no aminoquinoline can be obtained if the amides of lithium, sodium, or calcium are used. Potassium ammonobarate,  $\text{BaNK} \cdot 2\text{NH}_3$ , and quinoline also react to give aminoquinoline, presumably because of a slight dissociation of this salt into barium amide and potassium amide.

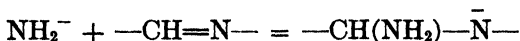
Isoquinoline reacts fairly rapidly with potassium amide in excess of one equivalent in liquid ammonia to form 1-aminoisoquinoline in yields as high as 83 per cent of the theoretical, together with hydrogen in somewhat larger quantity (5). If the isoquinoline is in excess of one molar proportion, the rate of formation of aminoisoquinoline is very slow. Therefore

<sup>6</sup> See section XVII A for the mechanism of the action of sodium amide with heterocyclic nitrogen bases and for the alkylation of 2- and 4-alkylquinolines.

it appears that an excess of amido ions,  $\text{NH}_2^-$ , is necessary for a rapid reaction, and since potassium amide is the only readily available amide of high solubility in liquid ammonia, it follows that very little, or no 1-aminoisoquinoline should be formed from isoquinoline and the sparingly soluble amides of sodium, lithium, calcium, and magnesium, as indeed proved to be the case. Barium amide, in spite of a low solubility in ammonia, did give 1-aminoisoquinoline in 54 per cent yield, together with hydrogen, and the reaction was found to be markedly accelerated by the ammonia-soluble barium thiocyanate. It is significant that aminoisoquinoline and hydrogen are formed even when isoquinoline is in excess. It therefore appears that barium (or barium ion, more probably) exerts the same catalytic effect here as in the reaction between quinoline and barium amide. Strontium amide is inferior to barium amide in the conversion of isoquinoline into 1-aminoisoquinoline.

The importance of an excess of  $\text{NH}_2^-$  ions in the potassium amide-isoquinoline reaction was tentatively explained in the following manner:

(1) An addition compound is first formed (cf. section X B)



(The  $\text{—CH=N—}$  group of isoquinoline is alone represented, and the reaction is written ionically.)

(2) An excess of amide ions favors the reaction expressed by the following equation, read from left to right,



(3) The influence of the two anionic charges on the nitrogen cause the removal of hydrogen and an electron, which ammonia converts to  $\text{H}_2$  and  $\text{NH}_2^-$ . In other words, potassium hydride is lost, as in the mechanism proposed by Ziegler and Zeiser for the sodium amide-pyridine reaction (168).

The ammono salts,  $\text{NaNK}_2 \cdot 2\text{NH}_3$  and  $\text{BaNK} \cdot 2\text{NH}_3$ , reacted with isoquinoline to give 1-aminoisoquinoline and hydrogen, but  $\text{CaNK} \cdot 2\text{NH}_3$ ,  $\text{SrNK} \cdot 2\text{NH}_3$ , and  $\text{Al}(\text{NH}_2)_2\text{NHK} \cdot \text{NH}_3$  failed to do so.

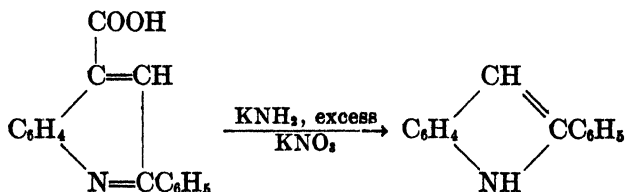
It has been shown experimentally (5, 7a) that isoquinoline and quinoline form addition compounds with the alkali amides in liquid ammonia. The potassium amide-quinoline addition compound, especially in the presence of an excess of  $\text{NH}_2^-$  ions, decomposes in time into resins, unless some reducible substance, such as potassium nitrate, is present (7a; see the first paragraph of this section).

2- or 4-Amino derivatives of homologues of quinoline are obtained by the action either of barium amide or of potassium nitrate and an excess of potassium amide in liquid ammonia on the substituted quinoline (7a).

Among other compounds, the following have been prepared: 4-amino-2-phenylquinoline in 92 to 100 per cent yield from 2-phenylquinoline; 4-aminoquinoline-2-carboxylic acid from quinoline-2-carboxylic acid (quin-aldinic acid); 2-aminoquinoline-4-carboxylic acid from quinoline-4-carboxylic acid (cinchoninic acid); the 2(?) -amino derivatives of 6- and 8-phenylquinoline, 6-dimethylaminoquinoline, quinoline-6-sulfonic acid, quinoline-6-carboxylic acid, and 6-methoxyquinoline (a mixture is obtained if potassium amide and potassium nitrate are used). In most of these reactions the second procedure has been of more value, since with barium amide solubility relationships are often of importance. 2-Phenylquinoline, for example, does not react with barium amide, although it reacts very rapidly with potassium amide and potassium nitrate.

Competition experiments have shown that quinoline-2-carboxylic acid and 2-phenylquinoline react more readily than quinoline with potassium amide and potassium nitrate in liquid ammonia, while 2-hydroxy- and 2-amino-quinoline are not attacked at all under the same conditions. Therefore reactions of this type are accelerated by phenyl and carboxyl but hindered by hydroxyl and amino (the effect of the methyl group has not been determined), contrary to what has often been observed when substituted benzenes are nitrated or sulfonated. (The  $\text{NH}_2$  group differs in polar character from  $\text{NO}_2$  (77).)

Cincophen (atophan, 2-phenylquinoline-4-carboxylic acid) undergoes a peculiar reaction with potassium amide and potassium nitrate in liquid ammonia at room temperatures, with the formation of 2-phenylindole (7a).

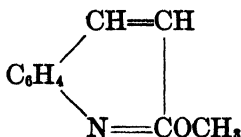


Since the latter is only formed when the water-soluble hydrolysate of the reaction product is boiled with water, it probably results by the ring closure of some intermediate. The reaction, the mechanism of which is at present unknown, is dependent in large measure upon the character of the substituents in the cinchophen. Thus, no indole derivative has been isolated by treating 2-*p*-tolyl-quinoline-4-carboxylic acid with potassium amide and potassium nitrate. 2-*p*-Methoxyphenyl indole, phenyl  $\alpha$ -naphthindole (= 2-phenyl-6,7-benzindole), and some others have been prepared by this reaction.

Quinoline-2-sulfonic acid is readily converted by a liquid ammonia solution of potassium amide at room temperatures into 2-aminoquinoline (74

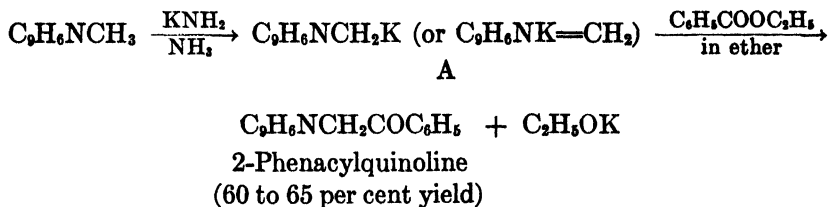
per cent yield), showing that a sulfonic acid group, as well as a halogen in position 2, has an enhanced reactivity (7a). A patent has recently been granted, in which it is stated that 2-aminoquinoline may be formed by heating quinoline-2-sulfonic acid with aqueous ammonia and zinc chloride (78a).

2-Methoxyquinoline,



is formally a cyclic neutral aquoammono ester, by virtue of the grouping  $-\text{C}(=\text{NR})\text{OCH}_3$ . It is therefore not surprising to find that a solution of potassium amide in liquid ammonia readily saponifies it to 2-aminoquinoline, the corresponding cyclic acid-ester of the ammonia system (64 per cent yield) (7a).

2-Methylquinoline, 2-methyl-5,6-benzoquinoline, and 2,3-dimethylquinoxaline react with potassium amide in liquid ammonia to give potassium salts, from which orange or yellow ketones may be obtained in a Claisen-type condensation, in accordance with the type equation,



For the purpose of convenience, the first step in the reaction is carried out in liquid ammonia, which is later evaporated and replaced by ether, although this latter solvent doubtless could have been used from the start. Two to three moles of potassium amide should be used for each mole of quinaldine, for otherwise the phenacylquinoline forms a potassium salt at the expense of the potassium quinaldyl (A), regenerating quinaldine.

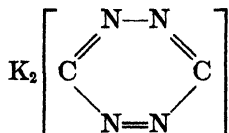
2-*p*-Methylphenacylquinoline, 2-*p*-methoxyphenacylquinoline, 2-*o*-chlorophenacylquinoline, 2-*p*-bromophenacylquinoline, 2-phenacyl-5,6-benzoquinoline, 2-*p*-methoxyphenacyl-5,6-benzoquinoline, 2-furoylquinaldine, and monobenzoyl-2,3-dimethylquinoxaline have been synthesized. Esters of aliphatic acids and many 2- or 4-alkylated quinolines whose potassium salts are insoluble in ether fail to react to give definite products (109).

Renfrew and Cretcher (123) were unable to introduce an amino group

into cinchonine or hydroquinine by means of sodium amide in boiling xylene. Instead there were obtained fairly good yields of the corresponding ketones, cinchinone (21 per cent) and hydroquinone (40 per cent).

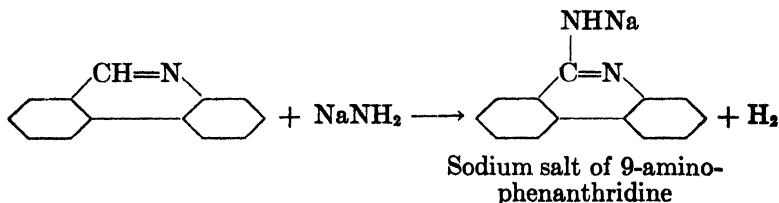
### E. Tetrazine

Tetrazine and potassium amide in liquid ammonia react to form a red dipotassium salt of the probable constitution (157; cf. 6, p. 163),



### F. Phenanthridine

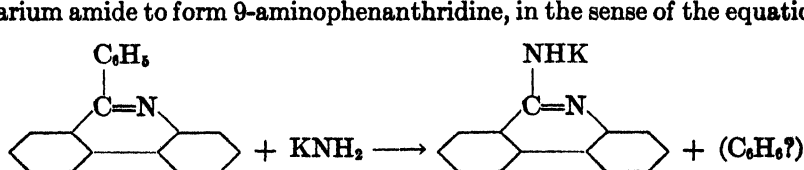
Morgan and Walls (110) made 9-aminophenanthridine by heating phenanthridine with sodium amide under xylene at 110–130°C., in accordance with the equation,



The average yield was about 60 per cent; the maximum yield 80 per cent.

Gee (50b) and Bergstrom (7a) have found that phenanthridine reacts with an excess of potassium amide in liquid ammonia to give hydrogen in almost quantitative yield and aminophenanthridine in quantities upward of 90 per cent of the theoretical. 9-Methylphenanthridine, like quin-  
aldine, reacts with potassium amide to form a potassium salt.

9-Phenylphenanthridine, since it contains the grouping  $\text{C}_6\text{H}_5-\overset{\text{R}}{\underset{|}{\text{C}}}=\text{N}-$ , is a cyclic ketone-ether of the ammonia system, and, as such, reacts with potassium amide, with potassium amide and potassium nitrate, or with barium amide to form 9-aminophenanthridine, in the sense of the equation,



The benzene has not been identified.

It will be recalled that benzophenone undergoes scission to benzamide and benzene when heated with sodium amide (6, p. 122).

## XIX. MISCELLANEOUS

Diphenyl selenoxide,  $(C_6H_5)_2SeO$ , and sodium amide react to give diphenylene selenide,  $C_6H_4-C_6H_4$ , and  $C_6H_5SeO_2$  (33; cf. 6, pp. 164-5,



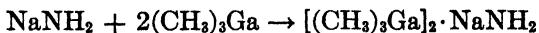
concerning the action of  $NaNH_2$  on  $(C_6H_5)_2SO$ ).

Kraus and Hawes (91) have prepared  $NaNH_2 \cdot B(C_6H_5)_3 \cdot 3NH_3$  and  $KNH_2 \cdot B(C_6H_5)_3 \cdot NH_3$  for conductivity measurements by treating boron triphenyl with sodium amide or potassium amide in liquid ammonia.

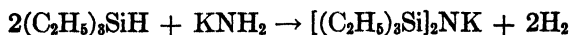
The preparation and use of alkyl substitution products of the alkali amides, such as  $(C_2H_5)_2NLi$  and cyclohexyl·NHNa, has been described in sections I, VI A and D, and XII C and F (161, 162, 163, 166, 167, 74, 3a).

Staudinger and Lohmann (139) find that sodium amide slowly polymerizes ethylene oxide to a product having a molecular weight of around 10,000 (two to three months reaction).

Kraus and Toonder (95) find that the reaction between sodium amide and trimethyl gallium in liquid ammonia follows the equation,

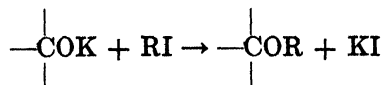


Although the methane hydrogen of triphenylmethane may readily be replaced by alkali metals, Kraus and Nelson (94) found that triethylsilicane undergoes the following peculiar reaction in liquid ammonia,

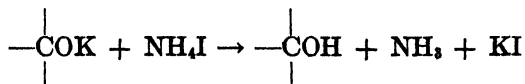
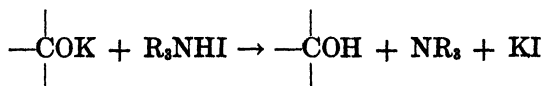
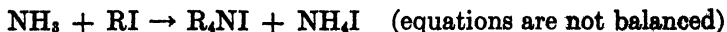


This recalls the reaction between the alkali amides and heterocyclic nitrogen bases of the type of pyridine, quinoline, and isoquinoline, in which amino derivatives are formed with the evolution of hydrogen (6, pp. 154-161; also section XVII A and B).

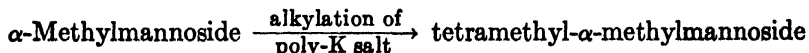
Muskat (112) prepared polypotassium salts of sugars in which the reducing group was suitably blocked by the action on them of potassium amide (or metallic potassium or sodium) in liquid ammonia at  $-33^\circ C$ . These salts react with methyl iodide, either in the presence or absence of solvent, to form methylated sugars, in sufficiently good yields to make this method valuable. The principal reaction is expressed by the equation,



but the following side reactions may occur:



As a general procedure, where the reactivities of the alkali metal salts of the carbohydrates and of the substituting reagent are unknown, it is advisable to remove the ammonia after the formation of the salt, and add the reagent in an inert medium. The following reactions are among those that have been carried out:



Miller and Siehrs (108) prepared monopotassium salts of the monosaccharides and dipotassium salts of the disaccharides by the action of potassium amide on concentrated liquid ammonia solutions of the sugars at  $-33^\circ\text{C}$ . As a rule these are stable in the air when dry, that is, when freed from solvent ammonia. Glycogen, however, gives a salt which chars on exposure to air. Reducing sugars are caramelized by potassium amide in liquid ammonia at room temperatures within a day, while sucrose is stable.

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*Errors in part II of the previous review (6)*

- p. 84. Middle of the page: change "potassium cyanide" to "sodium cyanide."
- p. 85. Bottom: change second line from bottom to read "cyanamide (as an alkali metal salt) is the only ammonocarbonic acid formed." Delete "disodium."
- p. 106. First line: after "phenyl group" add "attached to nitrogen."
- p. 109. Twelfth line: substitute "usually" for "often."
- p. 119. Third line above formulas: add (167) after "position." First line above formulas: substitute "(216, cf. 167)" for "(216)." Bottom two lines: change to read "... also causes a second radical to enter the  $\alpha'$ -position (166, 216b, as corrected by Cornubert and Humeau (Bull. soc. chim. [4] **49**, 1494-7 (1931))."
- p. 123. Eleventh line from bottom: substitute "hydrocarbon" for "hydrecarbon."
- p. 164. Section XVIII A, sixth line:  $S(=NH)$  is correct.
- p. 169. Reference 75: change "Ber. **26**" to "Ber. **36**."
- p. 170. Reference 170 should have "(1931)" in place of "(1921)."
- p. 173. Reference 216: designate the first reference (a) and the second (b).
- p. 175. Reference 270: change "(1913)" to "(1912)."



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